DISSERTATION

ON

STUDY OF PLASMA FIBRINOGEN IN ACUTE MYOCARDIAL INFARCTION

Dissertation submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfilment of the regulations

for the award of the degree of

M.D. -GENERAL MEDICINE- BRANCH – I

THANJAVUR MEDICAL COLLEGE,

THANJAVUR - 613 004.

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI - 600 032.

APRIL - 2013

CERTIFICATE

This is to certify that this dissertation entitled "**STUDY OF PLASMA FIBRINOGEN IN ACUTE MYOCARDIAL INFARCTION."** is the bonafide original work of **Dr. NARENDRAN.M** in partial fulfilment of the requirements for M.D Branch -I (General Medicine) Examination of the Tamilnadu Dr. M.G.R. Medical University to be held in APRIL - 2013. The period of study was from October– 2011 - November 2012.

Prof. Dr. C.GANESAN M.D.,
Unit Chief M-5
Department of Internal Medicine,
Thanjavur Medical College.
Thanjavur - 613 004.

Prof.Dr.S.MUTHUKUMARAN, M.D.
Head of the Department,
Department of Internal Medicine,
Thanjavur Medical College,
Thanjavur - 613 004.

Prof. Dr.C.GUNASEKARAN, M.D.,DCH.
The Dean I/C,
Thanjavur Medical College.
Thanjavur - 613 004.

Thanjavur Medical College

THANJAVUR, TAMILNADU, INDIA-613004

(Affiliated to the T.N Dr.MGR Medical University, Chennai)

ETHICAL COMMITTEE

CERTIFICATE

Name of the Candidate	:	Dr.M.NARENDRAN
Course	:	M.D (GENERAL MEDICINE)
Period of Study	:	OCTOBER 2011 – NOVEMBER 2012
College	:	THANJAVUR MEDICAL COLLEGE
Dissertation Topic	:	STUDY OF PLASMA FIBRINOGEN IN ACUTE MYOCARDIAL INFARCTION

The Ethical Committee, Thanjavur Medical College has decided to inform that your Dissertation Topic is accepted and you are permitted to proceed with the above study.

Thanjavur

Date :

THANJAVUR MEDICAL COLLEGE * THANJAVUR-4 *

Secretary

Ethical Committee

DECLARATION

I, **Dr.NARENDRAN. M**, solemnly declare that the dissertation titled **"DISSERTATION ON THE STUDY OF PLASMA FIBRINOGEN IN ACUTE MYOCARDIAL INFARCTION "** is a bonafide work done by me at Thanjavur Medical College, Thanjavur during October 2011 - November 2012 under the guidance and supervision of **Prof.Dr.C.GANESAN, M.D.,** Unit Chief M-5, Thanjavur Medical College, Thanjavur.

This dissertation is submitted to Tamilnadu Dr. M.G.R Medical University towards partial fulfilment of requirement for the award of **M.D. degree (Branch -I) in General Medicine**.

Place: Thanjavur.

Date: - 12 - 2012. **(Dr. NARENDRAN.M)**

ACKNOWLEDGEMENT

I gratefully acknowledge and my sincere thanks to The Dean I/C, **Prof.Dr.C.GUNASEKARAN, M.D.,DCH.,** Thanjavur Medical College, Thanjavur, for allowing me to do this dissertation and utilize the institutional facilities.

I am extremely grateful to **Prof.Dr.S.MUTHUKUMARAN M.D.,**Head of the Department, Department of Internal Medicine, Thanjavur Medical College, for his full-pledged support throughout my study and valuable suggestions and guidance during my study and my post graduate period.

I am greatly indebted to **Prof.Dr.C.GANESAN MD** my Professor and Unit Chief, who is my guide in this study, for his timely suggestions, constant encouragement and scholarly guidance in my study and post graduate period.

I profoundly thank my professors **Prof.Dr.P.G.SANKARANARAYANAN MD, Prof.Dr.K.NAGARAJAN M.D, Prof.Dr.S.MANOHARAN M.D. Prof.Dr.D.NEHRU MD DMRD,** and **Dr.C.PARANTHAKAN M.D.,** (Registrar), for their advice, guidance and valuable criticism which enabled me to do this work effectively.

I also express my heartiest thankfulness to my former unit chiefs **Prof.Dr.V.RAJENDRAN MD.,** & **Prof.Dr.M.SIVASANKARAN MD.,** for their advice and guidance.

I would like to express my gratitude to **Prof. DR.G. SENTHIL KUMAR , M.D., D.M..,** Department of cardiology and **Prof. DR. ARUMUGAM, M.D.,** Department of pathology for their immense help in the study which enabled me to complete this work and also permitting me to utilize the facilities available in the department.

My sincere thanks to assistant professors **Dr.GOWTHAMAN.G,M.D., Dr.SHRI RAM GANESH, M.D.,** and **DR.MAGESH.A, M.D.,** for their motivation, encouragement and support.

A special mention of thanks to all the patients who participated in this study for their kind cooperation.

I would like to thank my colleagues and friends who have been a constant source of encouragement.

INTRODUCTION

Cardiovascular disease is one among the major global health problems presenting in epidemic proportions. Myocardial infarction is one of the commonest cause of death, including low and middle income countries. India is in a transition phase from the state of high incidence of communicable disease to a state of high incidence of non communicable disease. India's contribution to the rising global burden of coronary artery disease is significant.[1]

High risks of coronary artery disease reported in south Asian populations, particularly in Indians regardless of the country in which they live.

During the last twenty years it is noted that Indians have a higher incidence of coronary artery disease. Myocardial infarction claims a large number of lives even before they reach fifth decade of life. Myocardial infarction occurring at early age is associated with absence of usual risk factors such as systemic hypertension, smoking, diabetes mellitus and hyperlipidemia in about one third of them.[2]

The coronary artery disease manifest as acute coronary syndrome including unstable angina, ST elevation MI and Non ST elevation MI. There is increase in mortality and complications associated with ST elevation MI.

turnitin

Your digital receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

Paper ID	291422654
Paper title	Dissertation on study of plasma fibrinogen in acute myocardial infarction
Assignment title	Medical
Author	Narendran 20101178 M.D. General Medicine
E-mail	dr.narendran.mani@gmail.com
Submission time	20-Dec-2012 03:45PM
Total words	8175

First 100 words of your submission

INTRODUCTION Cardiovascular disease is one among the major global health problems presenting in epidemic proportions. Myocardial infarction is one of the commonest cause of death, including low and middle income countries. India is in a transition phase from the state of high incidence of communicable disease to a state of high incidence of non communicable disease. India's contribution to the rising global burden of coronary artery disease is significant. 1 High risks of coronary artery disease reported in south Asian populations, particularly in Indians regardless of the country in which they live. During the last twenty years it is noted that Indians have a higher incidence of coronary...

ABSTRACT

BACKGROUND AND OBJECTIVES OF THE STUDY

Myocardial infarction is one of the commonest cause of death in the developing and developed countries. Indians are more prone to coronary artery disease but conventional risk factors do not explain the high rates of Coronary Artery Disease among Indians. Myocardial infarction is claiming a large number of lives in india. An impressive difference was absence of traditional risk factors in a third of them. Novel risk factors like homocysteine, lipoprotein (a), small LDL particle and fibrinogen may play a significant role in these patients. The aim of this study is to estimate fibrinogen levels in myocardial infarction patients and to study association of these novel risk factors with conventional risk factors.

METHODOLOGY

The present study included 70 patients who were admitted to IMCU and ICCU of Thanjavur medical college hospital during the period of Oct 2011–Nov 2012 fulfilling WHO criteria for acute myocardial infarction, presenting within 48 hours. Traditional risk factors were studied in addition to studying plasma fibrinogen levels.

RESULTS

This study was predominantly male oriented 49(80%). Mean age of the patients was 52.26 years. Chest pain was the most common presenting symptom present in all the patients followed by sweating 10 (14.3%). Dyslipidemia was the most

common 42 (60.9 %) risk factor in the present study followed by smoking 39 (55.7 %). High mean plasma fibrinogen (440.61 ± 75.4 mg/dl) levels was noted among patients. Significant association was noted between plasma fibrinogen and risk factors like dyslipidemia, obesity , diabetes and smoking . High plasma fibrinogen was observed in patients with chronic alcoholism, but not statistically significant.

INTERPRETATION AND CONCLUSION

In addition to the conventional risk factors of myocardial infarction, a high plasma fibrinogen levels were noted in patients with acute Myocardial infarction.

However, larger studies need to be done to substantiate these findings.

KEY WORDS: Myocardial infarction, Fibrinogen, Smoking, Dyslipidemia, Obesity.

CONTENTS

INTRODUCTION

Cardiovascular disease is one among the major global health problems presenting in epidemic proportions. Myocardial infarction is one of the commonest cause of death, including low and middle income countries. India is in a transition phase from the state of high incidence of communicable disease to a state of high incidence of non communicable disease. India's contribution to the rising global burden of coronary artery disease is significant.[1]

High risks of coronary artery disease reported in south Asian populations, particularly in Indians regardless of the country in which they live.

During the last twenty years it is noted that Indians have a higher incidence of coronary artery disease. Myocardial infarction claims a large number of lives even before they reach fifth decade of life. Myocardial infarction occurring at early age is associated with absence of usual risk factors such as systemic hypertension, smoking, diabetes mellitus and hyperlipidemia in about one third of them.[2]

The coronary artery disease manifest as acute coronary syndrome including unstable angina, ST elevation MI and Non ST elevation MI. There is increase in mortality and complications associated with ST elevation MI.

Acute myocardial infarction is due to sudden interruption of coronary blood flow. It is the complication of thrombotic occlusion of already narrowed coronary artery due to atherosclerosis.

The mortality following the acute coronary event depends on the size of the infarct. The left anterior descending supplies wide areas including bundle branches, ventricular wall and septum hence its occlusion results in larger area of infarct.

Salient features of coronary artery disease among Indians when compared to other ethnic groups.[3]

- More than two fold higher prevalence
- A decade earlier onset of first MI
- Nearly fivefold higher incidence of MI and mortality in younger population less than 40 years
- Severity of the disease
- Lower prevalence of traditional risk factors
- Higher prevalence of newer risk factors including fibrinogen, homocysteine, lipoprotein (a) and apolipoprotein B [3]

AIM OF THE STUDY

1. To study fibrinogen levels in subjects with acute myocardial infarction.
2. To compare the novel risk factors like fibrinogen with conventional risk factors like smoking, hypertension, diabetes mellitus, obesity and dyslipidemia.

REVIEW OF LITERATURE

Myocardial infarction

Definition

The World Health Organisation (WHO) definition includes the presence of two of the following[4]

1. Symptoms of myocardial infarction
2. Cardiac markers (enzymes) elevated
3. ECG showing characteristic electrocardiographic changes

Newer diagnostic criteria according to the American College of Cardiology and European Society of Cardiology.[5]

It requires the presence of one of the following diagnostic criteria to satisfy the diagnosis of acute, evolving or recent myocardial infarction.

1. Typical rise and gradual fall (troponin I/T) or more rapid rise and fall (CK-MBs) of biochemical markers of cardiac muscle necrosis with any one of the following:
   a. Symptoms of myocardial ischemia
   b. Appearance of pathological Q waves in ECG

c. ECG changes suggestive of ischemia (ST segment elevation / depression)

d. Coronary artery intervention (Eg. Coronary angioplasty)

2. Pathological findings of an acute Myocardial infarction

Risk factors

According to American heart association (AHA) prevention conference held in 1999, risk factors are classified to three categories.[6]

1. **Traditional /Conventional risk factors**.

- Cigarette smoking,
- Low HDL cholesterol
- Elevated serum cholesterol
- Hypertension
- Diabetes mellitus

2. **Predisposing factors**

- Male sex
- Physical inactivity
- Family history of CAHD
- Overweight & obesity
- Insulin resistance

3. Conditional factors

- Homocysteine
- Fibrinogen
- Small LDL particle
- C-reactive protein
- Lipoprotein (a)

Emerging risk factors

- Nitrotyrosine
- Oxidative stress
- Asymmetric dimethylarginine
- Myeloperoxidase

Smoking

Cigarette smoking is the one of the most important modifiable risk factor. It interacts with other risk factors to increase the risk multi fold. It accelerates coronary atherosclerosis in men and women, at all ages. Smoking increases the risk of thrombosis, plaque rupture, myocardial infarction, arrythmias and sudden death.

It increases the oxygen demand of myocardial tissue and hence worsens angina. Coronary artery disease causes about 40% of smoking related deaths, and in addition to it around 8% of them attributable to passive smoke exposure.

The most important and modifiable cause of coronary heart disease and death is smoking. Smoking correlates strongly with atherosclerotic disease , usually in association with other risk factors.[7]

It has been found that 28% of all deaths from coronary heart disease are attributed to tobacco smoking. Compared with non-smokers, current smokers have a 70% increased risk of fatal coronary event and a two to four fold increased risk of non-fatal CAD.[8]

In a recent major overview, smoking cessation reduced coronary heart disease mortality by 36% as compared with mortality in subjects who continued smoking.[9]

Smoking was the most common risk factor (87%) in a study by Siwach SB et al. who studied the profile of acute MI in young patients (below 40 years).[10]

Hyperlipidemia

Abnormalities in plasma lipoproteins and derangements in lipid metabolism rank as the most firmly established and best understood risk factor for atherosclerosis. The 4S trial demonstrated an approximately 40% reduction in incidence of myocardial infarction as well as a further reduction in the need of procedural intervention in hyperlipidemic individuals.[11]

In a study by Weinberger et al., hyperlipidemia was present in only four patients among 30 young patients.[12]

In a study by Kanitz et al., Hyperlipidemia was present in 20% of young adult patients.[13]

Hypertension

The elevated blood pressure has been shown to be associated with accelerated atherosclerosis and coronary heart disease. Elevated systolic blood pressure/diastolic blood pressure is clearly associated with an increased risk of coronary heart disease.[14]

In Framingham heart study even high normal blood pressure augements risk of cardiovascular disease two fold compared with lower levels.

Hypertension is not a common risk factor in CAD in young adults. In a study by Zimmerman FH et al., hypertension and diabetes were more frequent in older men and women.[15]

In study by Al Khadra et al., hypertension was documented in 18.5% of young individuals with acute myocardial infarction.[16]

Diabetes mellitus

Diabetes mellitus is the most important CAD risk equivalent. Most diabetic patients die of atherosclerosis and its complications.

The dyslipidemia present in diabetic patients is responsible for the elevated cardiovascular risk. The coronary artery disease is responsible for three fourths of all deaths in diabetic patients.[17]

There is endothelial and smooth muscle function impairment in diabetic patients. They also have increased adhesion of leukocytes to the vascular endothelial surface. This is very important step in atherosclerosis.

Patients with diabetes mellitus have two to eight fold higher rates of future cardiovascular events as compared with age and ethnically matched non-diabetic individuals.

In a study by Barbash GI et al. few young patients with MI had history of hypertension and diabetes mellitus.[18]

In a Nurse's health study, women who eventually developed type 2 DM, the relative risk of MI was increased 3 fold before the diagnosis of diabetes.[19]

In a study by Al khadra 30.8% of young patients with MI had diabetes mellitus.[16]

Gender

Men have increased risk of atherosclerosis than women. It is the most important predisposing factor for coronary atherogenesis. The female sex have protection from coronary atherogenesis. This effect is due to the estrogen. After menopause however, coronary risk accelerates in women.[20]

The Framingham study found a greater than two fold age adjusted increase in risk for CAD among post menopausal females compared with premenopausal females. Data from the Framingham cohort also indicate that there are sex specific differences in the manifestations of CAD.[21]

Male : Female ratio was 20:1, in study of profile of acute MI in young patients by Siwatch SB et al. [10]

Physical activity and Obesity

Regular physical activity is associated with cardio protective effect. It increases exercise capacity. It also reduces the oxygen demand of cardiac muscles. Hence it lowers the coronary risk. Cardioprotective effects of exercise include adiposity, diabetes incidence, lowered blood pressure, improved coronary endothelial function, lower CRP levels, and appears to benefit hemostatic variables including tissue plasminogen activator, fibrinogen, VWF, fibrin D dimer and plasma viscosity. [26]

A consistent series of prospective studies have demonstrated an association between levels of physical activity and reduced rates of cardiovascular mortality and morbidity.

In a prospective Harward study, those men with highest levels of activity at baseline had a 40% reduction in non-fatal cardiovascular events and 24% reduction in cardiovascular mortality compared with those with sedentary lifestyle.[22]

In the women health iniative, walking briskly for 30 mins, 5days/week associated with 30 % reduction in vascular events over a period of 3.5 years follow up.[23]

The American Heart Association has recommended an exercise energy expenditure approaching 2000 calories each week, a level of exercise that can be achieved with modest daily exertion.[24]

Recent studies indicate that waist / hip ratio, a surrogate marker for centripetal obesity is associated with coronary risk. This ratio holds good as a independent factor in both sex. [25]

Novel atherosclerotic risk factors [26]

Several newer risk markers of atherothrombotic risk are identified. They are proved by epidemiological studies. They are useful clinically. They are fibrinogen, lipoprotein (a), plasminogen activation inhibitor-1, homocysteine and high sensitivity C reactive protein.

C reactive protein

CRP is a acute phase reactant. CRP is a member of the pentraxin family. It plays important role in the human innate response. Apart from this effect , it directly affects vascular vulnerability. Levels of CRP greater than 3 mg/L also appears to predict recurrent coronary events.

Lipoprotein(a)

It was first described in detail by Berg et al. Its clinical importance was described by Mclean et al. They have structural similarity with apoprotien (a) and plasminogen.

It has LDL particle with apo B-100. This component is linked by a disulphide bridge to apoprotien (a).

Apoprotien (a) is member of a family of 'KRINGLE' containing proteins. Other members of this family include proteins such as Plasminogen, Prothrombin, Factor XII, urokinase type Plasminogen activator and Macrophage stimulating factor.

Lipoprotein(a) acts by binding on the endothelium. It competes with plasminogen. It binds to plasminogen receptor on endothelium. Thus it reduces the activity of plasminogen. Many epidemiological studies proves positive relation between lipoprotein(a) and atherogenic risk.

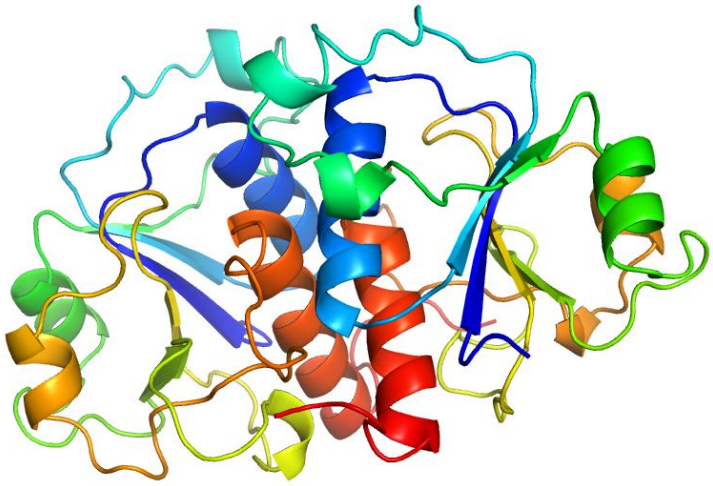
Their plasma concentration is inversely proportional to the size of apoprotein isoform. Thus small isoforms are associated with higher plasma Lp(a) concentration.

At birth Lp (a) levels are low and adult levels achieved in two years. Levels are high in asian and African population. Levels above 30 mg/dl are significant.

Serum Lp(a) levels elevated in type 2 DM, renal failure, menopause , hypothyroidism and malignancy. Height, weight, BMI, diet, weight loss and physical activity do not affect the level of serum lipoprotein (a).

HOMOCYSTEINE

Homocysteine was first described by botz and du vizwand in 1932, however a link to human disease was not suggested until 1962.



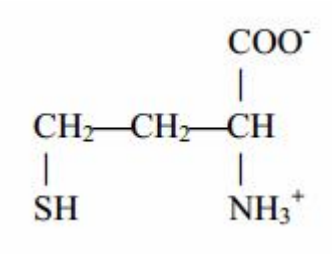
Structure of Homocysteine

The person who first described pre mature atherosclerosis in children and young individuals is Dr. McCully .In 1960s he demonstrated that atherosclerosis is present in children with disorders of homocysteine metabolism.

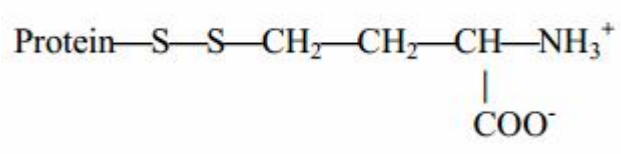
Dr. McCully demonstrated that atherosclerosis could be due to high homocysteine levels. He postulated the same cause for atherosclerosis in adults also. He hypothesized that elevated homocysteine levels is the cause for atherosclerosis, but this was not widely accepted. [27]

Homocysteine is a Intermediate derivative in the metabolism of methionine. This amino acid contains thiol containing group. Less than 1% circulates as free form (reduced state). Nearly 75% is bound to serum albumin. Around 25 % combines with other thiol containing amino acids or with itself to form dimer compounds. [28]

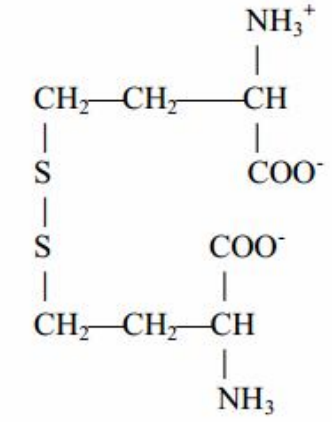
Homocysteine (reduced) 1%



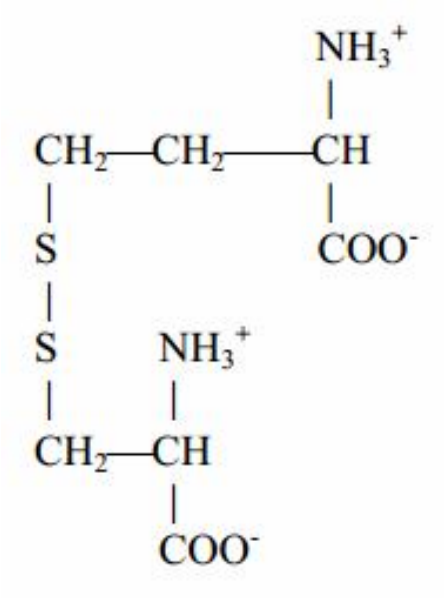
Protein bound homocysteine mixed disulphide (oxidised) 70-80%



Homocysteine (oxidised) 5-10%



Homocysteine- cysteine mixed disulphide (oxidised) 5-10%



Metabolism of homocysteine

The important 3 processes involved are as follows [28]

- Demethylation
- Transmethylation
- Transamination

Demethylation

In Demethylation methionine is converted to homocysteine .

In this process various intermediate metabolites are formed including S-adenosyl homocysteine & S-adenosyl methionine .

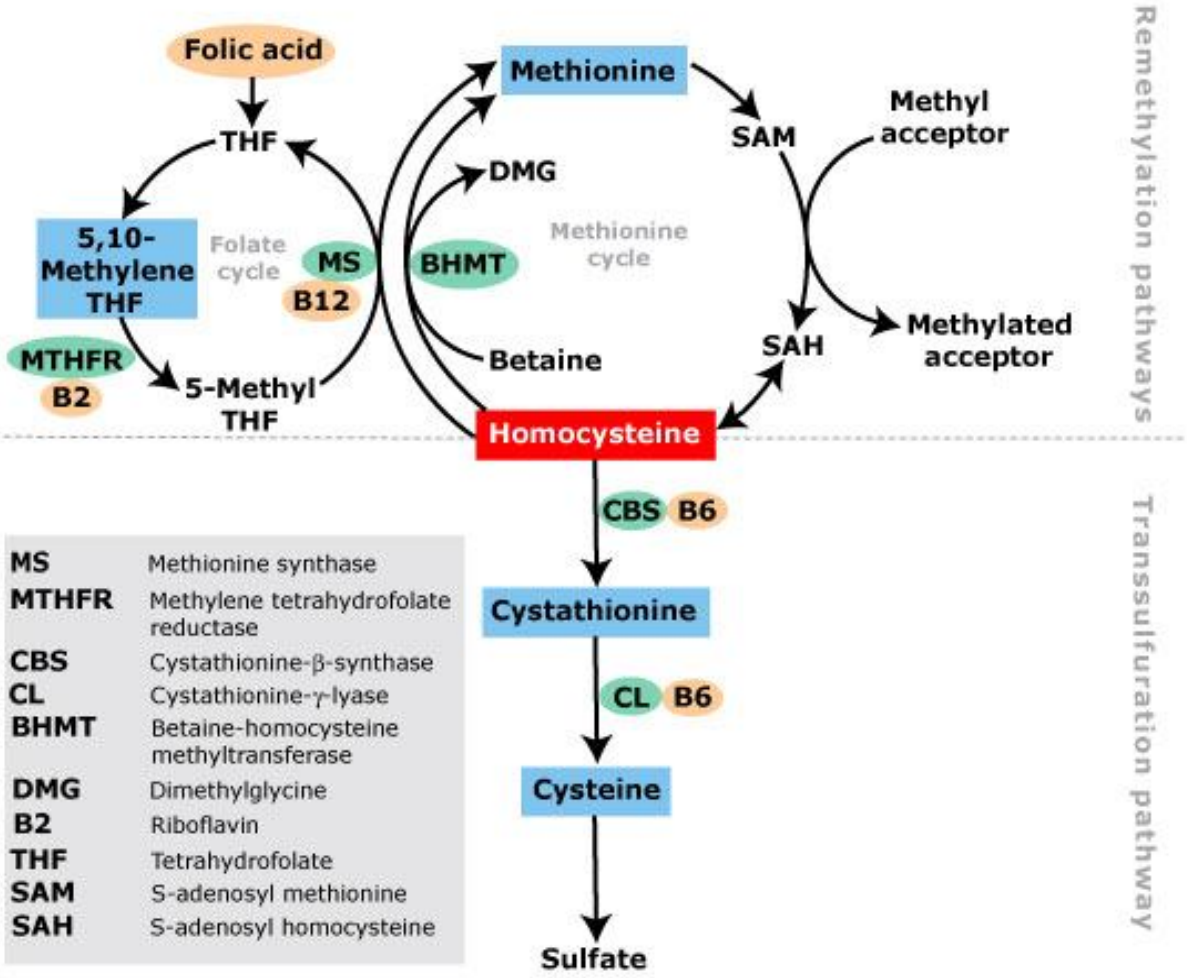


Fig. 1 : Metabolism of Homocysteine

This chart describes the metabolic pathways of Homocysteine in a nutshell. It describes both remethylation and transsulfuration pathways in our body.

Transmethylation

In transmethylation pathway homocysteine is again converted to methionine. Homocysteine is again remethylated to methionine in liver , by enzyme betaine-homocysteine methyl transferase. This step is catalysed by methionine synthase . Vitamin B12 is used as a co-factor. Methyl tetrahydrofolate acts as a substrate.

Transsulfuration

It is the process by which homocysteine is converted to cysteine. This reaction is irreversible process. In this pathway cystathionine β synthase which is vitamin B_6 dependent acts as catalyst. By this process cystathionine is formed as intermediate. Finally cystathionine is hydrolysed and it produces cysteine.

Measurement and Classification of Homocysteine Levels

The normal plasma homocysteine is 5-15 μmoles/L. Plasma homocysteine level greater than 15 μmoles/L is considered as hyperhomocysteinemia.

The American Heart Association have defined hyperhomocysteinemia as being divided into[29]

Moderate	**:**	**15-30 µmoles/L**
Intermediate	**:**	**30 - 100 µmoles/L**
Severe	**:**	**>100 µmoles/L**

Various methods of estimation of plasma homocysteine [30]

1 High liquid chromatography

2 ELISA

3 Mass spectrometry

4 Fluorescence polaraization immunoassay

Types of hyperhomocysteinemia

They are broadly divided into 2 types of hyperhomocysteinemia.[31]

1. Primary &
2. Secondary

1. Primary hyperhomocysteinemia

Due to defect in homocysteine metabolism pathways like:

a. Deficiency of Cystathionine beta synthase (CBS) :

It is the commonest cause of hyperhomocystinemia . It is transmitted as autosomal recessive trait. It occurs in frequency of 1 per 3 lakh live births.

The important clinical features are skeletal deformities, premature atherosclerosis , mental retardation and dislocation of lens . About one percent of the general population have cystathionine beta synthase deficiency, in heterozygous state. They have homocysteine levels elevated in the range of 20-40 micromol/L.

b. Deficiency of MTHFR (5,10 methylene tetrahydrofolate reductase)

The gene for enzyme MTHFR is mutated. It results in hyperhomocysteinemia associated with low folic acid.

c. Deficiency of Methylene tetrahydrofolate homocysteine methyl transferase [31]

2. Secondary hyperhomocysteinemia

a. Physiological

- Elderly age group
- Men
- Post menopausal

b. Modifiable factors

- use of Tobacco
- consumption of Coffee

c. Vitamin deficiency -

- Folate
- Vit B6 (pyridoxine),
- Vit B12 (cobalamine)

d. Systemic disorders

(i) Psoriasis

(ii) Anorexia nervosa

(iii) Systemic lupus erythematosus

(iv) Pernicious anaemia

(v) Hypothyroidism

(vi) Renal failure

(vii) Liver failure

(viii) Organ transplantation

e. Drugs (toxins)

1) Cholestyramine ,Colestipol ,Metformin (affect folate and cobalamin absorption)

2) Folate antagonists

- Phenytoin

- Carbamazapine

3) Vit B6 antagonists (Theophylline, Oestrogen containing OCP ,Niacin)

4) L-dopa (increases transmethylation)

5) Androgens

6) Cyclosporins ,Fibric acid derivatives (reduces renal function)

7) Nitrous oxide (inactivates methionine synthesis)

Determinants of plasma total homocysteine[32]

		Fasting plasma homocysteine
Sex	Male	10.3
	Female	8.8
Age (years)		
	< 45	8.8
	45-54	9.2
	54-64	9.8
	> 65	10.4
Serum creatinine (mol/L)		
	< 79	8.7
	79-87	9.3
	87-96	9.3
	96-106	9.7
	> 106	10.5
Alcohol intake (g/d)		
	0.1-4.9	9.3
	5-14.9	9.4
	> 15	10.0
Caffeine intake (mg/d)		
	< 88	8.9
	> 420	9.9
Current cigarette smoking		
	0	9.3
	1-15	9.9
	16-25	10.1
	≥ 26	11.0
Body mass index (kg/m2)		
	< 23.2	9.4
	≥ 30.6	9.9

Dietary intake of folate in a dose of 0.5 to 5 mg reduces homocysteine levels by 24 %. Vitamin B12 in addition reduces to about 7%.

Renal failure raises plasma homocysteine due to reduced renal clearance .

Coffee intake and smoking showed positive association with homocystiene. Moderate alcohol lowers while chronic alcoholics have increased plasma homocysteine.

Effects of Homocysteine on vascular endothelium [28]

It produces damage to vascular endothelial surface & accelerates atherosclerosis. It is also associated with thrombo embolism. It affects smooth muscle cells, coagulation factors, connective tissues , plasma lipoproteins and platelets. It also affects production of nitric oxide.

It stimulates the proliferation of vascular smooth muscule . It increases DNA synthesis and cyclin A. It causes platelet aggregation and increases platelet adhesion. The inhibition of Na+ - K+ - ATPase activity by Homocysteine is responsible for hemolysis of Red blood cells.

Hyperhomocysteinemia favours atherosclerosis [34]

Endotheial cell dysfunction is prerequisite for development of atherosclerosis. Homocysteine is toxic to endothelial cell surface by generating oxygen free radicals. Sulfydryl group reacts to ferric or cupric ions and gets oxidized to synthesis hydrogen peroxide. This reaction also produces oxygen free radicals and homocysteine radicals.

Homocysteine gets auto-oxidized to form Homocysteine mixed sulphides and homocysteine thiosulphates. There by it liberates hydrogen peroxide and superoxide anion. Hydrogen peroxide implicated in vascular injury of hyperhomocysteinemia.

The oxidation of LDL by Homocysteine causes vascular injury . Homocysteine thiolactone a byproduct oxidises native LDL. This step produces oxidised LDL which when taken up by intimal macrophages of vascular endothelium forms foam cells. This step initiates the early stage of atheromatous plaque formation. Homocysteine reduces synthesis of endothelial derived relaxing factor (NO). NO is a potent antiplatelet agent. It also inhibits production of hydrogen peroxide.

Hyperhomocysteinemia may interfere with antithrombotic and fibrinolytic mechanisms of the endothelium, making it prothrombotic. Homocysteine causes collagen deposition in atheromatous plaques . It also increases of proliferation of vascular smooth muscle cells .

Homocysteine decrease the activity of antioxidant enzymes. This effect is responsible for proliferation of smooth muscles of vascular endothelium by increasing their mitotic activity.

Complications of hyperhomocysteinemia[31]

- Hypertension
- Cerebrovascular accidents
- Ischemic heart disease
- Peripheral vascular disease
- Venous thromboembolism

Stroke and peripheral vascular disease

Their concentration is elevated in patients with CVA (stroke) and peripheral vascular disease (PVD) .

As regards cerebrovascular disease, eleven clinical studies looked at causal relationship between homocysteine levels and cerebrovascular disease. In nine studies, they have significant relationship while two prospective studies lacked evidence for an association.

Hyperhomocysteinemia and venous thrombosis

Hyperhomocysteinemia can be considered as a factor which favours venous thromboembolism.

Martin Den Haijer et al.[36] studied the plasma homocysteine concentration of patients with venous thrombosis. It was found to be elevated. The combination of hyperhomocysteinemia and factor V further increases the likelihood of venous thromboembolism .

Homocysteine and diabetes mellitus

Type 2 diabetes mellitus patients who had macrovascular disease had elevated homocysteine levels. It was shown that hyperhomocysteinemia appears to be a greater risk factor for cardiovascular disease in them, than the subjects with normal/impaired glucose tolerance.[37]

Homocysteine and hypertension

Bortolotto LA et al, demonstrated that hypertensive patients with elevated levels of homocysteine associates positively with arterial stiffness.[38]

Homocysteine and renal disease

Kidneys play an important role in homocysteine metabolism. Patients with renal failure have delayed clearance of homocysteine. This effect increases risk of atherosclerosis.

Homocysteine and ischaemic heart disease

As regards CAD, 17 studies were evaluated, out of which in 14 studies, homocysteine was found to be a significant risk factor. The CAD risk was around ten percent attributed to be due to elevated homocysteine. It was studied that reduction of homocysteine levels by 3 μmol/L results in 30% reduction of risk of ischaemic heart disease.[39]

Study done by Boushey et al. shows that increase in homocysteine levels is associated with an increased risk of peripheral arterial disease, ischaemic heart disease, CVA and venous thromboembolism.[40]

Studies by Arnesan et al illustrate that Homocysteine levels in study population was elevated than that of age and sex matched controls. This shows that ,it is an independent risk factor [41]

Nygard et al studied 587 angiographically documented cases. He showed that there is positive relation between between their elevated levels and mortality. [42]

In Asian Indians, Chacko did his studies with CAD and plasma homocysteine. He stated that plasma homocysteine could not be statistically proven in Asian populations. [43]

Chambers et al. studied UK Indian Asians with CAD and compared them with Europeans having CAD. They studied 764 male patients (257 Indian Asian and 507 European). Their results revealed that plasma homocysteine concentrations were higher in Indian Asians compared with Europeans. [44]

Ford et al, analyzed the prospective trails and concluded that there was 20% increase in cardiovascular risk for every 5 μmol/L increase in homocysteine levels.[45]

Enas A Enas et al found that women with homocysteine levels elevated above 16 μmol/L have double the risk of acute coronary event .[46]

Stampher et al, studied about coronary atherogenesis in doctors. His results are such that a rise in homocysteine concentrations ten to twelve percent is positively associated with three times the risk of acute coronary event. [47]

Homocysteine and aute coronary event in young adults

Myocardial infarction is claiming a large number of lives in young patients. Various studies have shown that homocysteine may be significant marker of risk in young patients lacking conventional risk factors .

In a study by ogawa et al, he discussed the role of homocysteine in myocardial infarction (young adults) and concluded that increased concentration of plasma homocysteine is absolutely a risk marker for myocardial infarction. [48]

Dr. Khare A. studied the role of homocysteine in patients with acute myocardial infarction less than 40 years age. He concluded that elevated homocysteine levels were independently associated with CAD. [49]

VK Katyal et al., studied 100 young patients(less than 40 years) admitted with acute MI and found hyperhomocysteinemia to be a significant contributor towards premature CAD.[50]

Study conducted by Puri A et al. showed that CAD is associated with homocysteine. He postulated that it can be taken as a important risk factor among young CAD patients.[51]

Stephen M Schwartz et al studied 79 women of age < 45 years diagnosed with MI and concluded that elevated plasma homocysteine and low plasma folate are risk factors for MI among young women.[52]

TREATMENT

The effective way of reducing homocysteine concentration in plasma is to treat with folates, vitamin B6 and B12. A strong negative correlation between folic acid levels and their homocysteine levels has been proven.

Guidelines of the American heart association advocate the principle of screen and treat, i.e., screening for hyperhomocysteinemia is recommended only in high risk population (personal or family history of premature atherosclerosis, myocardial infarction, hypertension, diabetes).

It is recommended to keep the homocysteine levels to <10μmol/L in the high risk group. Those with hyperhomocysteinemia should be treated with dietary modification followed by vitamin supplementation or fortification of food with vitamins (400 μgm of folic acid, 2mg of vitamin B6 and 6μgm of vitamin B12). [53]

In the vitamin intervention for prevention of stroke trial, the benefit of high dose vitamin therapy over vascular events was not established. The effect on stroke, CHD events, and death could not be proved. [54]

Results have shown that folic acid supplementation reduced plasma homocysteine by 41%, whereas Vit B12 supplement lowered homocysteine level by 14.8% and both were significant. But vit B6 therapy did not reduce homocysteine levels.

The combination of three vitamins reduced plasma homocysteine by 49.8%. [55]

FIBRINOGEN

It is a part of coagulation cascade. It regulates blood flow and viscosity.

Now studies shows that elevated plasma concentration of fibrinogen is associated with vascular events like CVA , thrombo embolic phenomenon and coronary artery disease.

Nevertheless, the role of fibrinogen in causing, atherosclerosis is complicated. The atheroma formation is similar in process to thrombogenesis. This step involves various other thrombogenic factors also. The major contributor is fibrinogen. Thus it has detrimental effects on vascular endothelium.

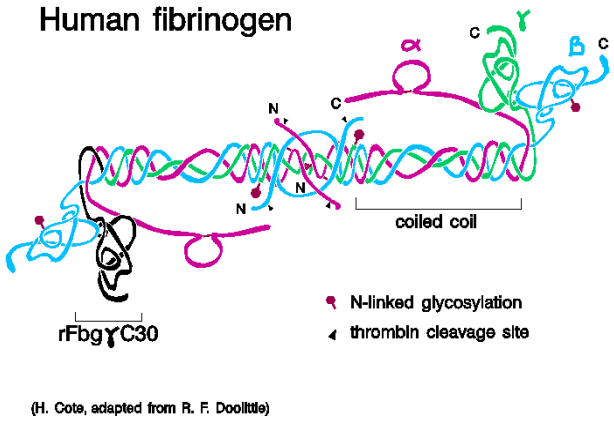


Fig. 2 : Schematic model of fibrinogen [56]

STRUCTURE OF FIBRINOGEN MOLECULE

The fibrinogen is a glycoprotein. Molecular weight around 340 kDa. Normal plasma concentration is 200 to 400n mg / dL. It is a precursor to fibrin. Length is 45 nm . Diameter 9 nm. It consists of three pairs of polypeptide chains . They are namely alpha, beta & gamma chains. They are held together by disulphide bonds.

The central nodule or E-domain is 5 nm in diameter and contains the NH2-terminal of all six polypeptide chains forming the NH2-terminal disulfide knot. The two outer D-domain nodules are composed of the C-terminal two thirds of both the Bβ and γ chains. Between the E- and D-domains, there is a stretch of approximately 120 amino acids from each of the three chains that forms an α-helical structure known as the coiled-coil domain. This region of the molecule is supported on both sides by a set of disulfide bonds called disulfide rings. These rings play an important role in making fibrin mechanically strong and resistant to proteolysis. Structural elements in each of the individual chains are needed for blood coagulation.

The Aα chain is a 610-amino acid polypeptide that can be divided into three distinct domains. The first section of the Aα chain (residues 1-194) contains a region (residues 45-161) linked to the Bβ and γ chains by disulfide bonds. This section forms part of the α-helix or coiled coil domain. This first section also contains fibrinopeptide A (residues 1-16) and the polymerization site in the E domain.

The Bβ chain is a polypeptide composed of 461 amino acids and is also divided into three sections. The first 80 residues contain the fibrinopeptide sequence (residues 1-15) and a site that supports endothelial cell spreading and proliferation (residues 15-42). The middle section (residues 81-192) is linked to the Aα and γ chains through disulfide rings and forms part of the coiled-coil domain.

The γ chain is only 411 amino acids long and is also divided into three distinct sections. Unlike the Aα and Bβ chains, there is no fibrinopeptide at the NH2-terminus of they chain.

The first 18 amino acids of the γ chain form part of the NH2-terminal disulfide knot, the middle segment of this polypeptide consists of amino acids 19-135. This section contains the disulfide rings that link this region to the Aα and Bβ chains in the coiled-coil domain.

There are 2 distinct forms of γ chains in human plasma fibrinogen. Approximately 15% of the γ chain contains an extended C-terminal and are designated γ' chains. Although Fibrin polymerization and cross linking of γ' proceed normally, the γ' chain does not support platelet aggregation. The clinical significance of the γ' chain remains unknown, however, recent studies suggest that γ' is a carrier for the zymogen of factor XIII in circulating blood.

Synthesis [57]

Plasma fibrinogen is synthesized in the liver by the hepatocytes. It is released into circulation with half life of nearly 100 hrs. it is degraded at rate of 24 % per day. The turnover rate of fibrinogen is about 1.7 to 5.0 gm/day.

Function[56, 57]

It is the clotting factor I, according to the system for naming blood clotting factors. It plays vital role in coagulation pathway. It produces fibrin on activation.

Results in fibrin which binds to lipoprotein and LDL and retains lipid moiety in the plaque. It is also important mediator in inflammation and atherogenesis. It plays pivotal role in thrombogenesis. The possible mechanisms include increased blood viscosity and enhanced platelet aggregation. It also causes atherothrombosis by infiltrating the vessel wall. Thus they favour thrombus formation.

Role in Inflammation

They interact with WBCs by 'integrins'.The integrins are surface receptors coated on the leukocytes.Mac1 and alpha X and beta 2 are the fibrinogen binding receptors.Mac1 is very specific for fibrinogen.

Fibrinogen also bind with intercellular adhesion molecule-1 (ICAM-1) . ICAM-1 is otherwise called CD54.It is present over vascular endothelium.

Fibrinogen attaches with Mac1 and also interacts with ICAM-1 to cause adhesion of monocytes over vascular endothelium. Fibrinogen also upregulates the expression of ICAM-1 or CD54 over the vascular endothelium.

Fibrinogen favours chemotaxis. Thus it is important in inflammation. This effect is mediated by binding with integrins receptors of leukocytes. As a consequence of this activation,the neutrophil activation markers are expressed. There is also increase in calcium concentration intracellularly.

Fibrinogen favours cell to cell adhesion and also facilitate cell to collagen (extracellular matrix). Thus it facilitates the inflammatory response.

Role in Thrombogenesis[58]

There is a normal balance between coagulation and fibrinolytic pathways.Thrombosis initiated when the balance fails.

Activation of Factor X to Factor Xa is the final step in coagulation pathway. This in turn converts prothrombin to thrombin. Thrombin facilitates conversion of fibrinogen to fibrin monomers. They adhere to each other to form fibrin clot.

Fibrinogen plays definite role in platelet aggregation . they interact with glycoprotein IIb-IIIa receptor present on platelets to facilitate its aggregation.

Role in Atherogenesis[58]

Fibrinogen plays pivotal role in causing endothelial damage. The fibrin formed upon activation of fibrinogen , initially acts over the intimal layer of the vessel wall and it promotes cellular proliferation.

They favour cell migration and cell adhesion. The fibrin degradation products are the main stimuli for chemotaxis, extracellular matrix synthesis and their proliferation. This affects the vascular permeability and their tone.

There is clear evidence for large amount of fibrin deposition in the atherosclerotic lesions in the human blood vessels. They are present either over the intact surface of plaque or buried within the fibrous cap.

Estimating fibrinogen levels [58]

It is done by two methods .

1. Functional methods

The Functional methods involves determining coagulation time. This is directly related to plasma fibrinogen concentration.Clauss method is widely accepted method. This is based on the time necessary for coagulation end point.

2. Direct method

This method quantifies the plasma concentration directly. They are based on immunological or gravimetric methods. The disadvantage is that they do not give information about quality of there function.

The normal plasma concentration varies circulating from 200 – 400 mg/dl. The widely accepted method is Clauss method.

Determinants of fibrinogen[59]

1. Genetics: There is genetic polymorphism which accounts for 30 to 50 percent variation.

2. Gender : According to Monica ausburgs,women generally have their fibrinogen levels elevated when compared with age matched men. This is irrespective of pregnancy. It is also independent of use of oral contraceptive pills.

3. Smoking : There is clear evidence for elevation of fibrinogen associated with smoking. There is proportional increase of 350mg/dl with each cigarette smoked. Smoking causes inflammation of pulmonary alveoli and bronchus. This inturn increases concentration of IL-6 which promotes synthesis of acute phase reactants from liver.

4. Alcohol : Mild to moderate alcohol intake reduces plasma fibrinogen levels. According to DESIR study, those who do not take alcohol or heavy drinkers taking more than 70gms/day have more plasma fibrinogen values..

5.Obesity : They have positive relationship with body mass index, waist hip ratio and waist circumference in both men and women.

6. **Exercise :** Regular physical activity reduces the level of fibrinogen. This effect attributes to the cardiovascular benefits of regular physical exercise.

7. **Hormonal Influence :** The use of oral contraceptive pills is associated with elevated fibrinogen levels

8. Age : Fibrinogen has a tendency to increase with age. This is attributed to the delayed clearance from plasma.

9. Role of Vitamins : Dietary intake of Vitamin C reduces plasma fibrinogen to a great extent.

10. Role of Infections: Certain organisms like Helicobacter pylori and Chlamydia were implicated in causing coronary artery disease.The role of fibrinogen may be explained following these infections. Its level is also increased in periodontal infections.

Factors increasing fibrinogen

- Old age, women
- African and asian race
- Over weight and obesity
- Smoking
- Post menopausal women
- Combined oral contraceptives
- Heavy alcohol drinkers
- Sedentary life style

Factors reducing fibrinogen

- younger age group
- Caucasians
- Japanese race
- Smoking cessation
- Low to moderate alcohol intake
- Regular physical activity
- Weight reduction

Role of Fibrinogen in acute coronary event

Many statistical analysis and prospective studies clearly shows that elevated plasma fibrinogen is associated with acute coronary event. This suggests the possibility of fibrinogen may be considered as a individual risk factor.[59]

In one meta analysis, which included a large number of prospective, cross sectional and case control studies concluded that the risk is about two times with elevated fibrinogen levels. Thus higher plasma levels are associated with increased risk of acute coronary event.[60]

In Framingham study, the cardiovascular risk is directly related to their plasma fibrinogen levels. The risk of acute vascular event increases with levels above 4.5gm/dl [61]

In European concerted action on thrombosis and disabilities study, they concluded that plasma fibrinogen can be taken as an independent risk factor. They provided it for acute coronary event as well as for sudden death. They also included measurement of plasma VWF and t-PA, in their studies.

The relationship with acute coronary syndrome is much stronger. This is proved statistically when compared with LDL cholesterol.[62]

Deepa et al, studied prothrombogenic risk factors in south Indian with CAD and found that prothrombogenic risk factors particularly fibrinogen may be associated with CAD.[63]

Fibrinogen and young MI

Khare A et al. studied fibrinogen levels in 120 patients with MI less than 40 years of age and concluded that fibrinogen is an independent risk factor.[49]

Von Eyben et al. studied fibrinogen levels in 22 patients with MI aged less than 41 years, came to conclusion that fibrinogen was independent risk factors.[64]

Elikowski W et al, studied thrombotic risk factor in 40 young survivors [aged 30-40 yrs] of myocardial infarction and found high fibrinogen levels among them.[65]

Lewandowski k et al, studied 99 male patients aged less than 40 yrs with MI and found that the frequency of BcII polymorphism of the beta-fibrinogen gene was significantly higher in MI patients along with higher plasma concentration of fibrinogen.[66]

Interventions to reduce its level

Several drugs lower plasma fibrinogen concentrations, including some beta adrenergic blocking agents, platelet inhibitors, and fibric acid derivatives, but lifestyle modifications such as exercise and modest alcohol intake may be the most satisfactory initial treatment of choice.[67]

Intervention to decrease plasma fibrinogen [59]

The most successful in reducing plasma fibrinogen levels includes drugs like fibrates, plasmapheresis, alcohol intake and most importantly by stopping smoking.

The other steps which yield doubtful benefits include hormone replacement in post menopausal women, weight reduction, lowering hypertension etc., Statins are not useful.

According to Bezafibrate Coronary Atherosclerosis Intervention Trial (BECAIT), the benefit of therapy is mediated by fall in fibrinogen levels.[68]

MATERIALS AND METHODS

SOURCE OF DATA

Cases for the present study were selected from the inpatients of ICCU ward, IMCU ward in Thanjavur medical college Hospital, Thanjavur between Oct 2011 to Nov 2012.

METHOD OF COLLECTION OF DATA

Sample size: 70 cases

Present study involved 70 patient admitted to Thanjavur medical college Hospital with diagnosis of acute myocardial infarction. A detailed history and thorough clinical examination was done as per the proforma and were investigated further.

Inclusion Criteria

1. Patients fulfilling WHO criteria for acute myocardial infarction .
2. At least two of the three elements presenting within 48 hours
   a. History of ischemic chest discomfort
   b. Typical ECG changes
   c. Elevated cardiac enzymes

Exclusion Criteria

1. Patients with renal dysfunction/ Liver disease
2. Patients with thyroid disease.

The following parameters were studied

Smoking : Proper history of smoking obtained in terms of pack years & smoking index

Diabetes mellitus

1. Known diabetics and their duration of disease.
2. Newly detected DM satisfying WHO criteria
   a. Symptoms of diabetes mellitus with random blood glucose >200 mg%
   b. Fasting plasma glucose > 126 mg%,
   c. 2 hr plasma glucose > 200 mg%

Hypertension

1. Known hypertensives on treatment and their duration of disease
2. Newly detected hypertension according to JNC VII criteria

Family history of Ischemic heart disease

Obesity : Patients were classified accordingly as overweight and obese based on body mass index. BMI = Weight (kg)/height (mt^2)

Obesity - BMI > 30

Over weight - BMI 25 to 30

Dyslipidemia

According to NCEP-ATP III guidelines, patients were considered to have dyslipidemia when

1. Total cholesterol > 200 mg%,
2. HDL < 40 mg%,
3. LDL > 100 mg%
4. Triglycerides > 150 mg%.

Plasma fibrinogen level : The levels were measured quantitatively by Coagulation method done by SYSMEX 500 series. Serum fibrinogen values greater than 400 mg/dl is considered as hyperfibrinogenemia.

Other investigations

ECG

RBS,

Blood urea

Serum creatinine

Cardiac enzymes – CKMB

Method of Statistical Analysis

The data were analysed by calculating percentages, mean values, standard deviation and standard error using one-sample T test, independent samples, chi-square T test and ANOVA – one way test.

All statistical calculations were performed using the software SPSS for windows 14 evaluation version.

RESULTS

In this study 70 patients with evidence of acute myocardial infarction were evaluated. Novel risk factor fibrinogen studied in comparison with other conventional risk factors.

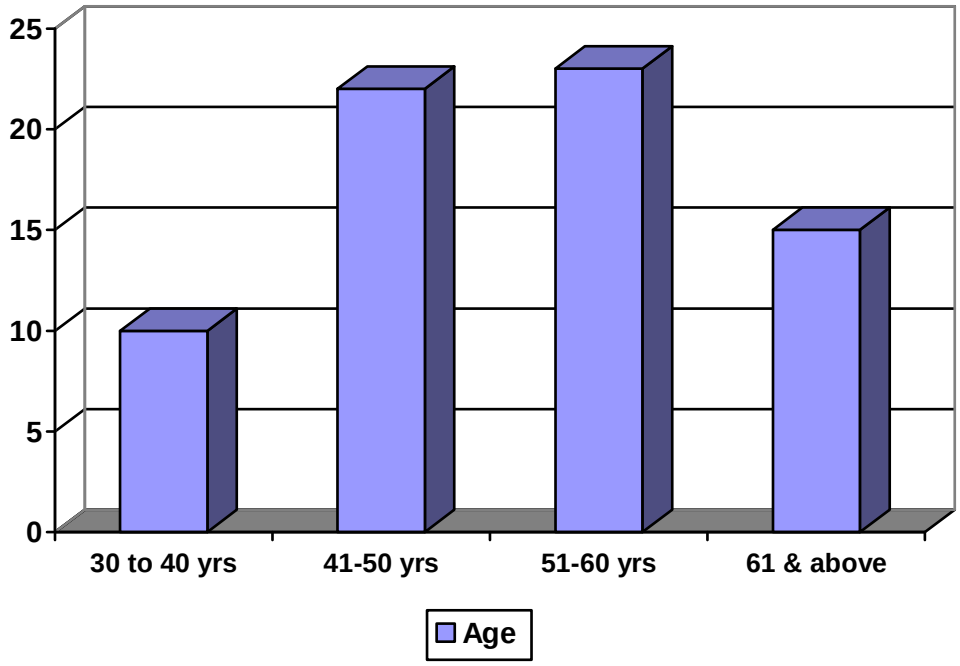
Table – 1 : Age wise Distribution of the cases

Sl.no	Particulars	No.of respondents (n=70)	Percentage (100%)
1	30 to 40yrs	10	14.3
2	41 to 50yrs	22	31.4
3	51 to 60yrs	23	32.9
4	61 & above	15	21.4

In this study most of the cases were between the age group of 51 to 60 years. Youngest patient in this study was 30 year old.

Mean age among the cases was 52.26 years

Chart 1 : Age wise distribution of the cases



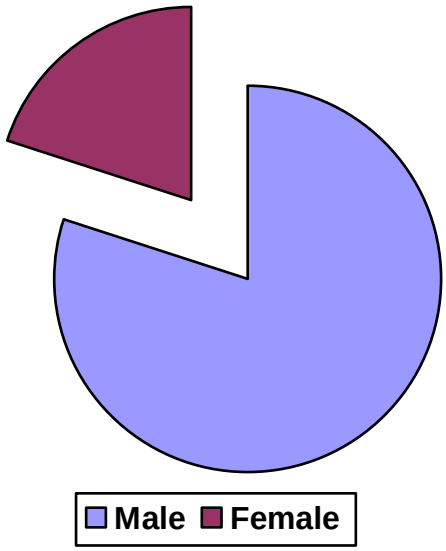
This graph shows age wise distribution of cases . Most of cases were in the age group 51 to 60 in our study.

Table – 2 : Sex wise Distribution of the cases

Sl.no	Particulars	No.of respondents (n=70)	Percentage (100%)
1	Male	56	80.0
2	Female	14	20.0

This was a male dominated study with males comprising 80% of the study group.

Chart 2 : Sex wise Distribution of the cases



This pie chart illustrates the sex wise distribution of cases. In our study males contribute to around 80% of cases.

Table - 3 : Difference between gender of the respondents and their P.fibrinogen

T Test

Sl.no	P.fibrinogen (mg%)	Mean	S.D	Statistical inference
1	Male (n=56)	439.54	72.104	T=-.238
2	Female (n=14)	444.93	90.308	.813>0.05 Not Significant

Df=68

Statistical test: Student 't' test was used the above table

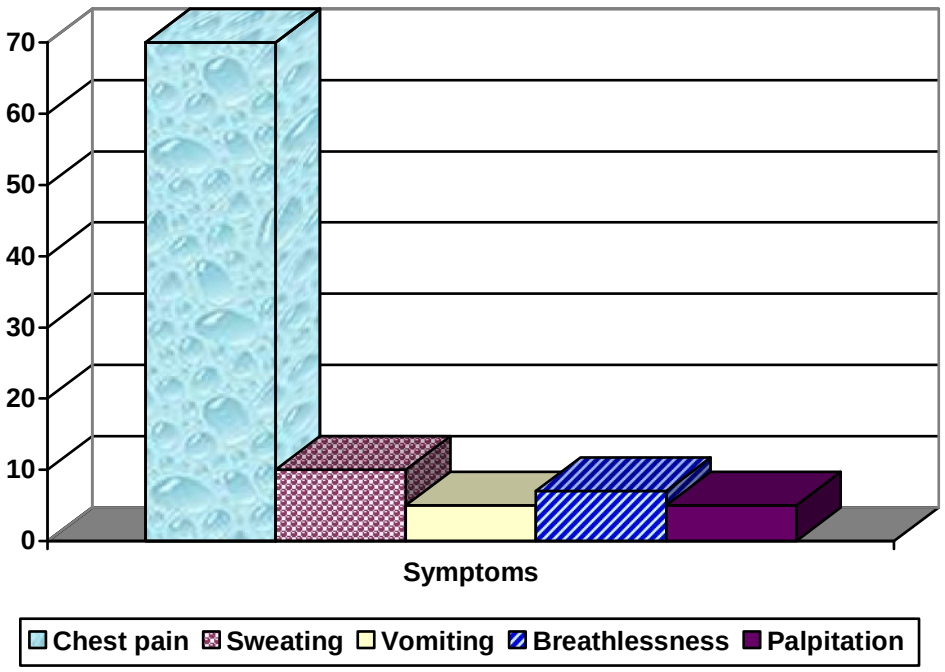
In our study the mean plasma fibrinogen of females is higher than males . But this is not statistically significant.

Table – 4 : Symptoms at the time of admission

Symptoms	Number of cases	Percentage
Chest Pain	70	100
Sweating	10	14.3
Vomiting / Nausea	5	7.1
Breathlessness	7	10
Palpitation	5	7.1

Chest pain was the most common symptom which was present in all patients (100%) followed by sweating (14.3%)

Chart 3 : Symptoms at the time of admission



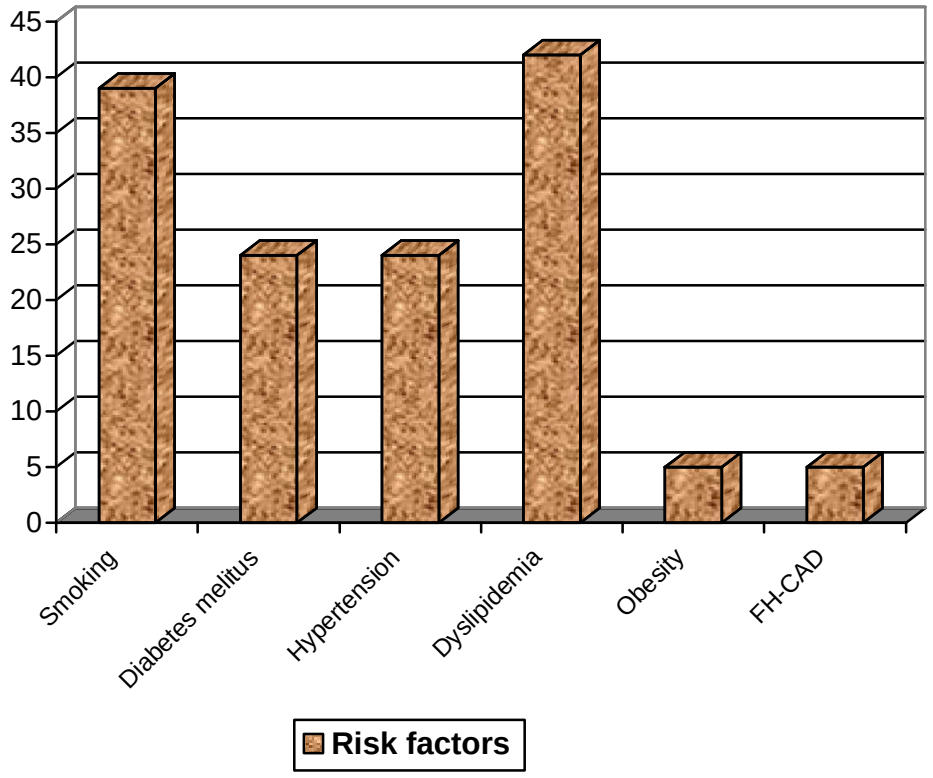
This bar diagram shows symptom wise distribution of cases. In our study most common symptom is chest pain.

Table –5 : Comparison of risk factors among patients

Risk Factors	Number of Cases	Percentage
Dyslipidemia	42	60.9
Smoking	39	55.7
Diabetes Mellitus	24	34.3
Hypertension	24	34.3
Obesity	5	7.1
F H – C A D	5	7.1

In this study dyslipidemia (60.9%) was the most common risk factor followed by smoking (55.7%). Diabetes mellitus and hypertension were observed in 24 number of patients. Overweight was present among 50 % of patients and only 5 (7.1%) patient was obese. 34.3% of the study group were alcoholics.

Chart 4 : Comparison of risk factors among patients



This bar chart shows the risk factor wise distribution of cases. In our study dyslipidemia is the most common risk factor (60 .9 %) , followed by smoking (55.7 %).

Table –6 : Percentage of cases with hyperfibrinogenemia

Risk factors	Number of Cases	Percentage
Fibrinogen	47	67.1

In this study significant number of patients (67.1%) had hyperfibrinogenemia.

Chart 5 : Percentage of cases with hyper fibrinogenemia

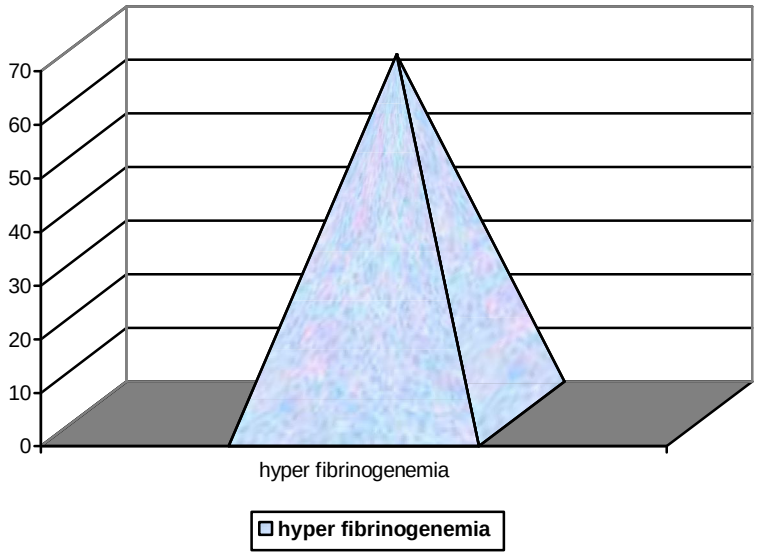


Table –7 : Study of plasma fibrinogen levels in our patients

T-Test

Study of level of P.fibrinogen of the respondents

Sl.no	P.fibrinogen (mg%)	Mean	S.D	Statistical inference
1	<400 (n=23)	352.78	41.974	T=-11.847
2	>400 (n=47)	483.60	44.054	.000<0.05 Significant

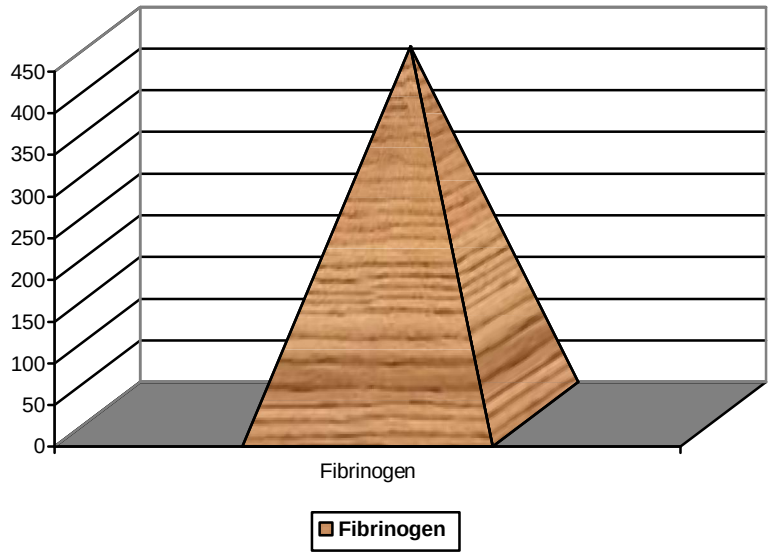
Df=68

Statistical test: Student 't' test was used the above table

Risk factors	Mean Values	P value
Fibrinogen (Normal 180-400 mg/dl)	440.61± 75.4 mg/dl	0.000<0.05

In this study mean plasma fibrinogen level was (440.61± 75.4 mg/dl), which was high compared to the normal fibrinogen levels and was statistically significant.

Chart 6: Mean plasma fibrinogen in our study



This chart shows mean plasma fibrinogen in our study (440.61 mg/dl)

Table – 8 : Comparison of mean plasma fibrinogen levels among smokers and non-smokers

	Smokers	Non – smokers	P value
Fibrinogen (mg/dl)	433.64± 72.08	421.3± 71.02	0.035<0.05

Mean fibrinogen level (433.64mg/dl) was high among smokers when compared to non-smokers (421.3mg/dl), and was statistically significant

Chart 7 : Comparison of mean plasma fibrinogen level among smokers and non smokers.

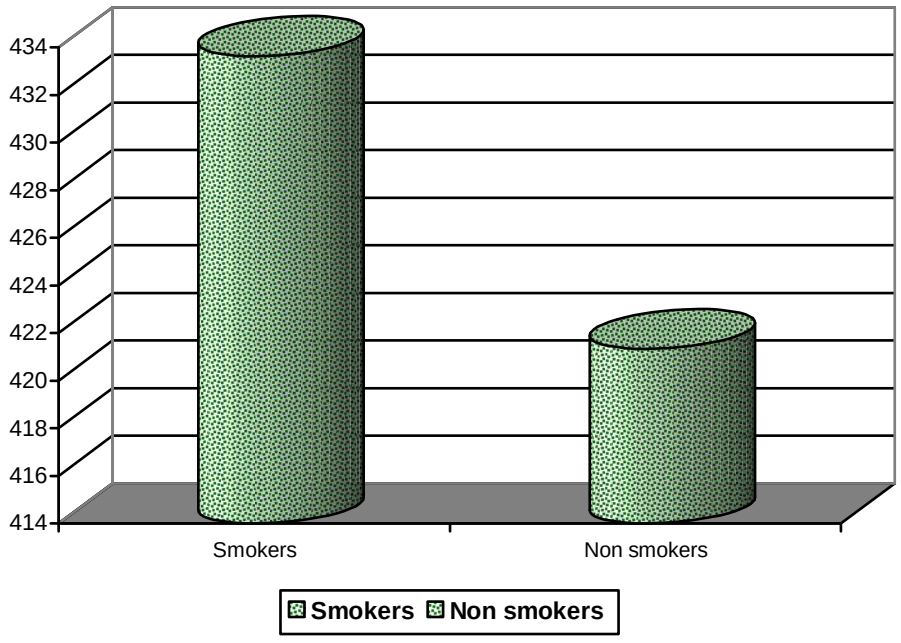


Table – 9 : Comparison of mean plasma fibrinogen levels among diabetics and non diabetics

	Diabetics	Non – Diabetics	P value
Fibrinogen (mg/dL)	463.33 ± 77.31	428.76± 72.4	0.046<0.05

Diabetics had higher values of fibrinogen (463 mg%) when compared to non-diabetics (428 mg%) , which was statistically significant. (p value 0.046 < 0.05) .

Chart 8 : Comparison of mean plasma fibrinogen levels among diabetics and non diabetics

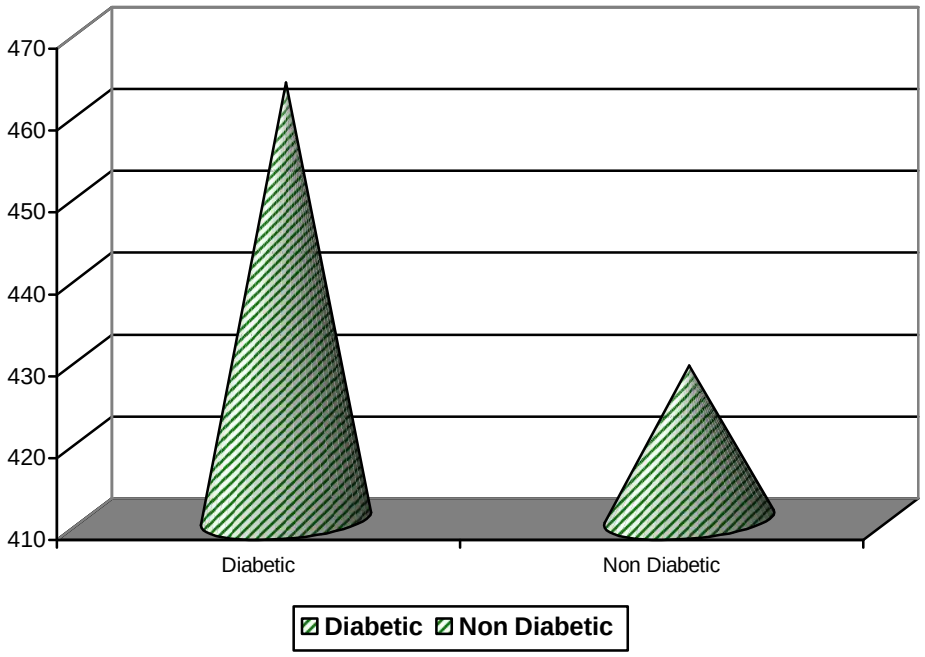


Table-10 : Comparison of mean plasma fibrinogen among hypertensives and non hypertensives

Sl.no	P.fibrinogen (mg%)	Mean	S.D	Statistical inference
1	Hypertensive (n=24)	452.13	78.751	T=.922
2	Non hypertensive (n=46)	434.61	73.759	.360>0.05 Not Significant

Df=68

Statistical test: Student 't' test was used the above table

The mean plasma fibrinogen in hypertensives (452.13 mg/dl) was high when compared with non hypertensives (434.61 mg/dl), but this difference is not statistically significant.

Chart 9: Mean plasma fibrinogen among hypertensives and non hypertensives

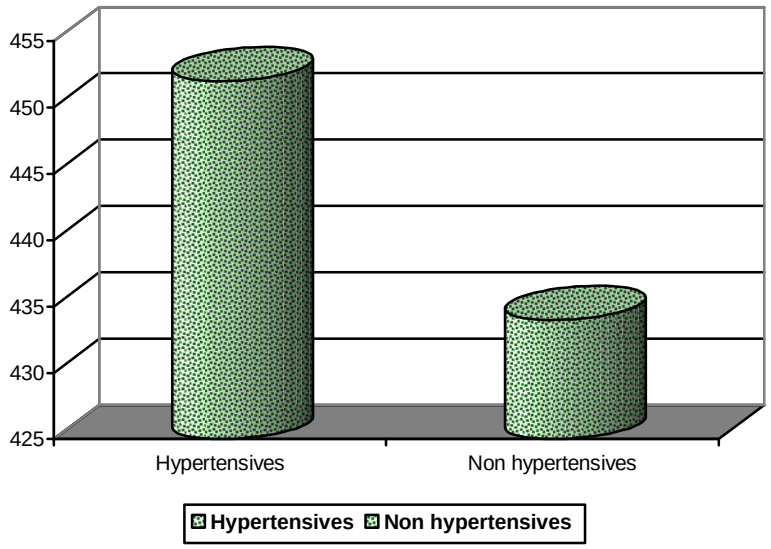


Table 11: Comparison of mean plasma fibrinogen of alcoholics and non alcoholics

Oneway ANOVA difference between alcohol of the respondents and their P.fibrinogen

Sl.no	P.fibrinogen (mg%)	Mean	S.D	SS	Df	MS	Statistical inference
1	Between Groups			11616.973	2	5808.486	F=1.022 .365>0.05 Not Significant
2	Nil (n=46)	446.85	75.419				
3	CR (n=13)	443.69	56.696				
4	OCC (n=11)	410.91	92.815				
5	Within Groups			380677.613	67	5681.755	

Statistical test: Oneway ANOVA ‘f’ test was used the above table

The mean plasma fibrinogen of chronic alcoholics is higher than occasional alcoholics , but it is not statistically significant.

Table – 12 : Comparison of mean plasma fibrinogen levels among patients with high LDL level and patients with normal LDL

Sl.no	Particulars (LDL mg %)	No.of respondents (n=70)	Percentage (100%)
1	Below 100	28	40.0
2	100 to 129	26	37.1
3	130 to 159	11	15.7
4	160 & above	5	7.1

Sl.no	P.fibrinogen (mg%)	Mean	S.D	SS	Df	MS	Statistical inference
1	Between Groups			7622.973	3	2540.991	F=4.436 .031<0.05 Significant
2	Below 100 (n=28)	428.86	79.774				
3	100 to 129 (n=26)	449.15	73.408				
4	130 to 159 (n=11)	453.00	69.146				
5	160 & above (n=5)	454.80	67.059				
6	Within Groups			384671.613	66	5828.358	

Subjects with high LDL (> 100 mg %) had their Plasma fibrinogen Concentration (445. 65 mg %) higher than persons with normal LDL (428.86 mg %)

Chart 10 : Comparison of mean plasma fibrinogen levels among patients with dyslipidemia and patients with normal lipids

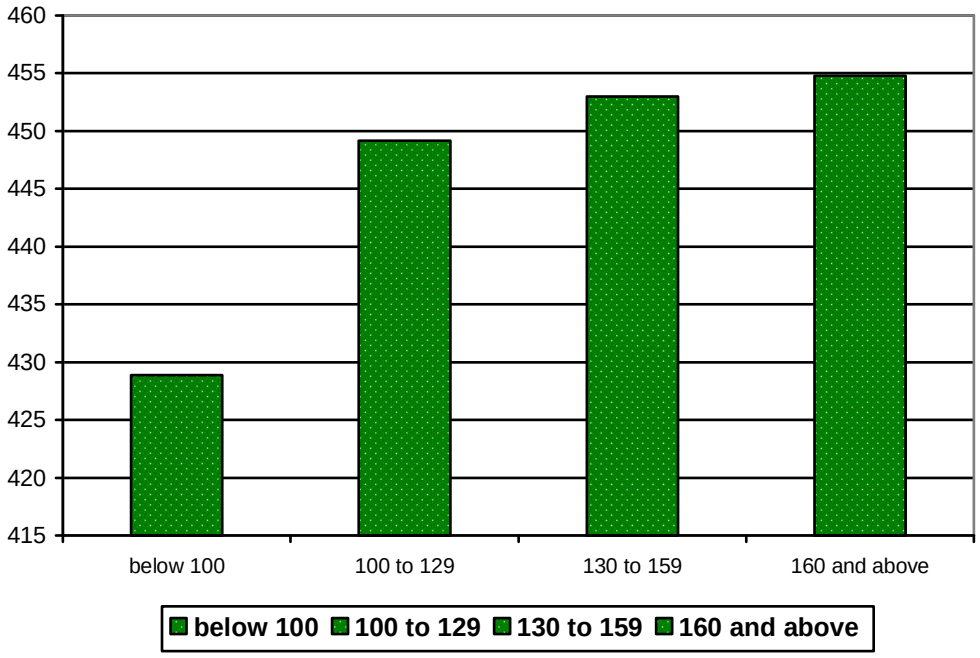


Table 13 : Comparison of HDL level and mean plasma fibrinogen

T-Test

Difference between level of HDL of the respondents and their P.fibrinogen

Sl.no	P.fibrinogen (mg%)	Mean	S.D	Statistical inference
1	Less than 40 (n=15)	456.20	82.755	T=.902
2	More than 40 (n=55)	436.36	73.507	.601>0.05 Not Significant

Df=68

Statistical test: Student 't' test was used the above table

In our study subjects with HDL level above 40 mg/dl ,their plasma fibrinogen level is lower . But this difference is not statistically significant.

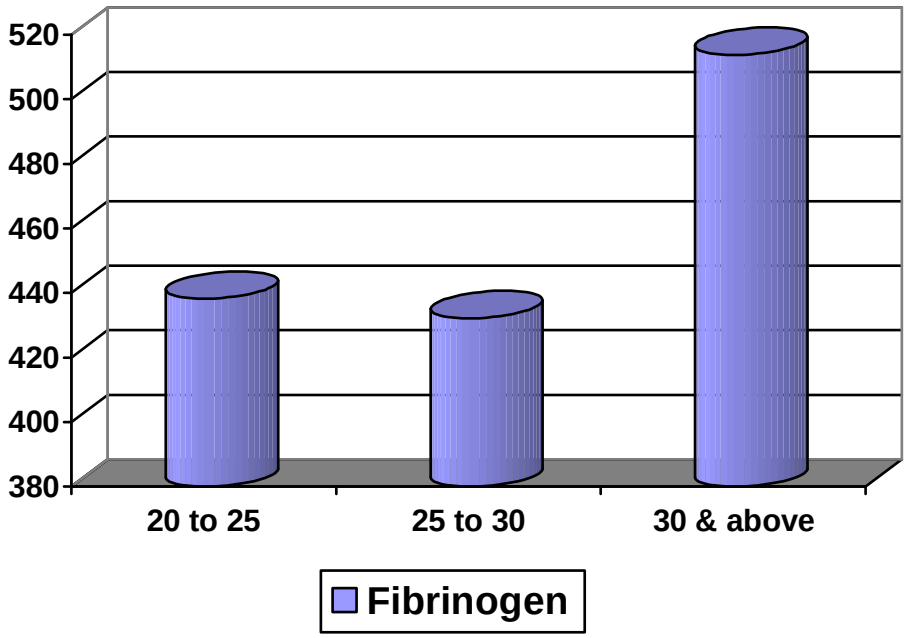
Table – 14 : Comparison of mean fibrinogen levels among patients with obesity and patients with normal BMI

Sl.no	Particulars	No.of respondents (n=70)	Percentage (100%)
1	20 to 25	30	42.9
2	25 to 30	35	50.0
3	30 & above	5	7.1

Sl.no	P.fibrinogen (mg%)	Mean	S.D	SS	Df	MS	Statistical inference
1	Between Groups			29428.819	2	14714.410	
2	20 to 25 (n=30)	438.23	73.520				F=4.717
3	25 to 30 (n=35)	432.20	77.393				.043<0.05
4	30 & above (n=5)	513.80	24.823				Significant
5	Within Groups			362865.767	67	5415.907	

The mean plasma fibrinogen in BMI < 25 is 438.23 mg/ dl . The mean plasma fibrinogen in BMI between 25 to 30 is 432.20 mg /dl. In obese group plasma fibrinogen is around 513.80 mg/dl. The difference is statistically significant.

Chart 11 : Comparison of mean fibrinogen levels among patients with obesity and over weight and patients with normal BMI



This chart describes the correlation between BMI and the plasma fibrinogen of the study group which is statistically significant.

DISCUSSION

70 patients of with evidence of acute MI admitted to ICCU and IMCU were studied and the following data were compared.

Table - 15 : Comparison of sex wise distribution of the cases

Study	Males %	Females %
SK mishra et al[69]	90	10
Khare A et al[49]	91.67	8.33
AL Khadra et al[16]	96.9	3.1
Ranjit N[72]	86	14
Present Study	80	20

Sl.no	Particulars	No.of respondents (n=70)	Percentage (100%)
1	Male	56	80.0
2	Female	14	20.0

The study was predominantly male (80%) dominated. This may be attributed to the protective effects of estrogen in pre-menopausal women. This was comparable to the other studies.

Table - 16 : Comparison of age wise distribution of the cases

Sl.no	Particulars	No.of respondents (n=70)	Percentage (100%)
1	30 to 40yrs	10	14.3
2	41 to 50yrs	22	31.4
3	51 to 60yrs	23	32.9
4	61 & above	15	21.4

In our study, mean age of the patients was 52.26 years.

Most of the patients were in the age group between51 to 60 years (32.9%).

Study	Age (Mean) in years
Present Study	52.26
Romero M et al[50]	56.4
Hampten et al[71]	57.03

Table – 17 : Comparison of symptoms at admission

Symptoms	Mishra SK et al.[69]	Patil CN et al.[71]	Present Study
Chest Pain	83.4%	93.3%	100%
Sweating	61%	50%	14.3%
Vomiting / Nausea	5%	16.7%	7.1%
Breathlessness	29%	16.7%	10%
Palpitation	-	3.3%	7.1%
Stroke	0.8%	-	-
Syncope	6%	-	-

In our study chest pain (100%) was the most common symptom followed by sweating (14.3%). Similar findings were noted in study by Mishra et al and Patil et al .

Table - 18 : Comparison of risk factors

Risk Factors	Al. Khadra et al[16]	Puri et al[70]	Mishra SK et al[69]	Present Study
Dyslipidemia	33.8%	58.8%	52%	60.9%
Smoking	76.9%	52%	75%	55.7%
Diabetes	30.8%	21.5%	16.5%	34.3%
Hypertension	18.8%	54.9%	23%	34.3%
Obesity	15.4%	23.3%	37%	7.1%
F H – C A D	-	-	33.8%	7.1%

Dyslipidemia (60.9%) was the most common risk factor which was comparable with other studies, Al. Khadra et al (33.8%), Mishra et al (52%).

In our study smoking is present in 55.7 % and 7.1 % patients are obese. Other risk factors like hypertension, Diabetes mellitus and family history of CAD were present in a few patients.

Table - 19 : Comparison of mean plasma fibrinogen level with other studies

Study	Mean Fibrinogen (mg /dl)
Cristal N et al[49]	466 ± 89.5
Puri et al[50]	447.68 ± 142.35
Romero M et al	457 ± 46.22
Present study	440.61± 75.40

High mean plasma fibrinogen (440.61 ±75.40 mg/dl) level was noted which is statistically significant. This is comparable with other studies .

Comparison of mean plasma fibrinogen levels with conventional risk factors

1) Smoking

Mean plasma fibrinogen was high among smokers (433.64 mg/dl) compared to non smokers (421 mg/dl) and was satistically significant.

Kannel WB et al.,[73] in Framingham study noted higher values of fibrinogen among smokers.

2) Dyslipidemia

Patients with dyslipidemia had higher mean plasma fibrinogen (445.65 ±73.48 mg/ dl) compared to patients with normal lipid levels (428.86 ± 79.77 mg/dl). Puri et al.[70] noted high fibrinogen levels among patients with dyslipidemia when compared to patients with normal lipids.

3) Over weight and obesity

Significantly higher levels of fibrinogen was noted among patients with BMI > 30 (513.8 mg/dl) when compared to patients with normal BMI (438.23 mg/dl). Difference was statistically significant.

Craveri et al [74] noted significantly higher plasma fibrinogen among patients with BMI > 30 compared to those with BMI < 25.

4) Alcohol

Significantly high levels of fibrinogen was noted among chronic alcoholics (443.44mg/dl) compared to occasional alcoholics (344.78 mg/dl). Mennen LI et al[76] in DESIR study found that moderate alcohol consumption was associated with lower plasma fibrinogen when compared with those who were non drinkers or who drinks >60gm of alcohol per day.

5) Hypertension and Diabetes

High levels of fibrinogen was noted among patients with hypertension but was not statistically significant. Higher levels associated with diabetic patients is statistically significant.

CONCLUSION

- In our study males contribute around 80% of cases.
- All patients presented with chest pain.
- Dyslipidemia was the most common conventional risk factor followed by smoking
- Novel risk factors like fibrinogen were elevated in myocardial infarction patients in our study group when compared to normal levels.
- Significant number of patients in our study had hyper fibrinogenemia.
- Significant association was noted between fibrinogen and risk factors like Dyslipidemia , Obesity and Smoking
- Large scale randomized multicentre studies are yet to be done to understand the proper association between novel risk factors like fibrinogen with myocardial infarction.

SUMMARY

In this study 70 patients with acute myocardial infarction were studied.

- Most of the patients were males (80%).
- Majority of the patients were between the age group of 41-60 years (64.3%).
- All patients presented with chest pain. Sweating was present in 14.3% of patients.
- Dyslipidemia was the most common risk factor, which was present in 60.9% of patients followed by Smoking (55.7%). Few number of patients had hypertension, diabetes and family history of coronary artery disease.
- The mean fibrinogen level was (440.61 ± 75.40 mg/dl) which was high compared to normal fibrinogen level.
- Smokers had higher mean fibrinogen level compared to non smoker and was statistically significant.
- Mean fibrinogen level was high among patients with high LDL and was statistically significant.
- Plasma fibrinogen was high among diabetics and was statistically significant.

- Hypertensive patients had higher fibrinogen levels when compared to non hypertensive patients, but was not statistically significant.
- Patients with overweight and obesity had higher levels of mean fibrinogen levels and was statistically significant.
- Patients who were chronic alcoholics had higher levels of fibrinogen when compared to occasional alcoholics.

BIBLIOGRAPHY

1. WHO Disease statistics. World health report 1999.Mortality by sex ,cause and WHO regions, estimates for 1998.
2. Enas A Enas, Jatinder Dhawan, Sanjiv Puthar. Coronary Artery Disease in Indians. Indian Heart J 1997; 49 : 25-34.
3. Singh SP, Sen P. Coronary heart disease. The changing scenario. Indian J Prev Soc Med 2005; 34: 71-81.4.
4. Luepker RV, Apple FS, Christenson RA, et al. Case definition for acute coronary disease in epidemiological and clinical research studies. Circulation 2003; 108: 2543.
5. Alpert JS, Thygeson K, Antman E. Myocardial infarction redefined: A consensus document of The Joint European Society of Cardiology /American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol 2000; 36: 959.
6. Grundy SM, Pasternak R, Greenland P et al, Assessment of cardiovascular risk by use of multiple risk factor assessment equations, American college of cardiology. Circulation.1999 ;100: 1481-1492
7. Bastecehi CE, Mackenzic TK, Schnir RW. The human cost of tobacco use. N Eng J Med 1994; 330: 907-912, 975-980.

8. Jonas MA, Oates JA, Ockene JK. Statement on smoking and cardiovascular disease for health care professionals: AWA Medical/ Scientific Statement. Circulation 1992; 86: 1669.
9. Critchley JA, Capewell B, Mortality risk reduction associated with smoking cessation in patients with CAD. JAMA 90; 86: 2003.
10. Siwach SB, Singh H, Sharma D. Profile of young acute myocardial infarction in Haryana. J Assoc Physicians India 1998; 47(6): 654.
11. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: The Scandenavian Simvastatin Survival Study (4S). Lancet 1994; 344: 1383-1389.
12. Weinberger I, Rotenberg Z, Fuchs J. Myocardial infarction in young adults under 30 years: Risk factors and clinical course. Clin Cardiol 1987; 10(1) :9-15.
13. Kanitz MG, Giovannucci SJ, Jones JS. MI in young adults; Risk factors and clinical features. J Emerg Med 1996; 14(2): 139-45.
14. Wibon PW, D'Agostino RB, Levy D. Prediction of coronary heart disease using risk factor categories. Circulation 1998; 1837-1847.
15. Zimmerman FH, Cameron A, Fisher LD. Myocardial infarction in young adults: Angiographic characterization, risk factors and prognosis. J Am Coll Cardiol 1995; 26(3): 654-61.

16. Al khadra AH. Clinical profile of young patients with acute myocardial infarction in Saudi Arabia. Int J Cardiol 2003; 91(1): 9-13.
17. Gu K, Gowic CC, Haris MI. Mortality in adults with and without diabetes in a national cohort of the US population. Diabetes Care 1998; 21: 1138-45.
18. Barbash GI, White WD, Modan M. Acute myocardial infarction in young the role of smoking. Eur Heart J 1995; 16(3): 295-6.
19. Hu FB, stampher MJ, Haffner SM,et al ; Elevated risk of cardiovascular disease prior to clinical diagnosis of type 2 diabetes . Diabetes Care 2002; 25: 1129.
20. Wenger NK, Speroff L, Pachard B. Cardiovascular health and disease in women. N Engl J Med 1993; 329: 247-256.
21. Lerner DJ, Kannel WB. Patterns of coronary heart disease morbidity and mortality in the sexes; A 26 year follow up of the Framingham population. Am Heart J 1986; 113: 383-90.
22. Paffen RS, Hyde RT, Wong AL, Berger B. Physical activity, all cause mortality and longevity of college alumni. N Engl J Med 1986; 314: 605-613.
23. Manson JE, Grrenland, P,Lacriox AZ et al; Walking compared with vigorous exercise for the prevention of cardiovascular events in women. NENG J Med 2002; 347: 716.

24. Fletcher GF, Balady G. Exercise standards: A statement for health care professionals from the American Heart Association. Circulation 1995; 91: 580-615.
25. Rurode KM, Casey VJ. Abdominal adiposity and coronary heart disease in women. JAMA 1998; 280: 1843-48
26. Paul M.Ridker, Peter Libby ; Risk factors for atherothrombotic disease; \In: Braunwald E, Zipes DP, Libby P (eds), Heart disease-A textbook of cardiovascular medicine. 7th ed. Philadelphia, USA: Elsevier Saunders 2005; p. 946-953.
27. McCully KS. Vascular pathology of homocysteine ; Implication for the pathogenesis of arteriosclerosis. Am J Pathol 1969; 56: 11-28.
28. Kailash Prasad. Homocysteine, a risk factor for cardiovascular disease. International Journal of Angiology 1999; 8: 76-86.
29. Malinow MR, Bostom AG, Krauss RM. homocysteine, diet, and cardiovascular diseases, a statement for health care professionals from the nutritional committee, American heart association. Circulation 1999; 99: 178-82.
30. Ebba Nexo, Frode Engback et al. Evaluation of novel assays in clinical chemistry–quantification of plasma total homocysteine. Clinical Chemistry 2000; 46(8): 1550-1556.

31. Neki NS. Hyperhomocysteinemia-An independent risk factor for cardiovascular diseases Indian Heart J 2001; 53: 44-47.
32. Paul FJ, Bostom AG, Peter WF, Rich S, Irwin HR and Jacob S. Determinants of plasma total homocysteine concentration in the Framingham offspring cohort. Am J Clin Nutr 2001; 73: 613-21.
33. Homocysteine lowering trialists collaboration, lowering blood homocysteine with folic acid based supplements: meta analysis of randomized trials, BMJ 1998: 316: 894-98.
34. Sainani GS, Sainani R. Homocysteine and its role in the pathogenesis of atherosclerotic vascular disease. J Assoc Physicians India 2002; 50: 16-23.
35. Clarke R, Daly L, Robinson K, et al. Hyperhomocysteinemia, an independent risk factor for vascular disease. N Eng J Med 324;1149-1155
36. Heijer M, Kostor T. Is hyperhomocysteinemia a risk factor for recurrent venous thrombosis ; Lancet 1995; 345: 882-5.
37. Hoogeveen EK et al. hyperhomocysteinemia is associated with an increased risk of cardiovascular disease, especially in noninsulin dependent diabetes mellitus. A population based study. Arterioscl Thromb Vasc Biol 1998; 18: 133-138.
38. Bortolotto LA et al .plasma homocysteine, aortic stiffness and renal function in

hypertensive patients. Hypertension 1999; 34: 837-42.

39. Tambe AB. Homocysteine and atherosclerotic vascular disease. Cardiology Today 2000; 4: 269-71.

40. Boushey CJ, Beresford SAA, Omenn GS et al. A quantitative assesment of plasma homocysteine as a risk factor for vascular disease. J Am med Assn 1995;274: 1049-1057.

41. Arnesen E. Serum total homocysteine and coronary heart disease. Int J Epidemiol 1995; 24: 704-9.

42. Nygard O, Nordrehaug JE, refsum H, et al. Plasma homocysteine levels and morality in patients with CAD . N Eng J Med 1997; 337: 230-236.

43. Chacko KA. Plasma homocysteine levels in patients with coronary heart disease. Ind Heart J 1995; 23: 36-40.

44. Chambers JC, Obeid OA, Refsum H. Plasma homocysteine concentrations and risk of coronary heart disease in UK Indian Asian and European Men. Lancet 2000; 355: 523-7.

45. Ford ES, Smith SJ, Stroup DF, et al. homocysteine and cardiovascular disease. Int J Epidemiol 2002; 31: 59-70.

46. Enas A Enas, Senthilkumar A, Vijaya Juturu, et al. Coronary artery disease in women. IHJ 2001.

47. Stampfer MJ, Malinow MR, Willett WC. A prospective study of plasma

homocysteine and risk of myocardial infarction in US physicians. JAMA 1992;268: 877-81.

48. Ogawa M, Abe S, Saigo M, Biro S, et al. Homocysteine and hemostatic disorder as a risk factor for myocardial infarction at a young age. Thromb Res 2003; 109(5-6): 253-8.

49. Khare A, Ghosh K, Shetty S, Kulkarni B, Mohanty D. Combination of thrombophilia markers in acute myocardial infarction in young. Indian J Med Sci 2004; 58(9): 381-388.

50. Katyal VK, Siwach SB, Jagdish, Singh S. Homocysteine levels in young myocardial infarction patients (<40 years). J Assoc Physicians India 1998; 46(5): 424-6.

51. Puri A, Gupta OK, Dwivedi RN, Bharadwaj RPS, Narain VS, Singh S.

52. Homocysteine and lipid levels in young patients with coronary artery disease. J Assoc Physicians Ind 2003; 51: 681-685.

53. Stphen M, Schwartz, David S Sisccovick, et al. Myocardial infarction in young Women in relation to plama homocysteine, folate, and a common variant in the MTHFR gene. Circulation 1997; 96: 412-417.

54. Omena GC, Beresford SAA, Motulsky AG. Preventing coronary heart disease ; Bvitamins and homocysteine . Circulation 1998 ; 97: 421-24.

55. Toole JF, Malinow MR, Chambless le et al. Lowering homocysteine in patients

with ischemic stroke to prevent recurrent stroke, myocardial infarction, and death; Vitamin intervention for stroke prevention randomized controlled trial. JAMA 2004; 291: 565-575.

56. Ubbink J, Vermaak W. Vitamin supplements for the treatment of hyperhomocysteinemia in humans. J Nutr 1994; 124: 1927-23

57. Richard GL. Wintrobe's Clinical haematology. 10th ed. Philadelphia, USA: Lee and Febiger 2002; 717-719.

58. Hoffman R. Hematology basic principles and practice. 2nd ed. Philadelphia, USA: WB Saunders 1998; p. 1703-1713.

59. Kamath S, Lip GYH. Fibrinogen: Biochemistry, epidemiology and determinants. QJ Med 2003; 96: 711-729

60. Ernest E, Resch KL, et al. Fibrinogen as a cardiovascular risk factors. A meta analysis and review of literature. Ann Intern Med 1993.

61. Maresca G, Di Blasio A, Marchioli R, et al. Measuring plasma fibrinogen to Predict stroke and MI. Arterioscles Thromb Vasc Biol 1999; 19: 1368-77.

62. Kannel WB, Wolf PA, castelli WP et al. Fibrinogen and risk of cardiovascular disease. The Framingham study JAMA 1987; 258: 1183-1186.

63. Thompson SG, Kinast J, Pyke SD, et al, Hemostatic factors and the risk of

MI or sudden death in patients with angina pectoris .N Eng J Med 1995; 332: 635-41.

64. Deepa R, Velumurugen K, Saravanan G, et al. Relationship of tissue plasminogen activator and plasminogen activator inhibitor I and fibrinogen with CAD in south Indian male subjects. JAPI 2002; 50: 901-906.

65. Von Eyben FE, Mouritsen E, Holm J, et al. Smoking, low density lipoprotein, cholesterol, fibrinogen and myocardial infarction before 41 years of age: a Danish case-control study. J Cardiovasc Risk 2002; 9(3): 171-8.

65 Elikoski W, Zozolinske M, Psoja P, et al. Evaluation of thrombotic risk in a young men after myocardial infarction during a period of clinical stability. Pol Arch Med 1992; 88(6): 401-10.

66. 66 Lewandowski K, Kwasnikowski P, Elikowski. W, et al. Myocardial infarction in patients aged less than 40 years. Frequency of bcII polymorphism in the fibrinogen beta-chain gene and plasma fibrinogen. Kardiol Pol 2003; 59(9): 205-12

67. Ernst E, Resch KL. Therapeutic intervention to lower fibrinogen concentration. Eur Heart J 1995; 16: 47-53.

68. Faire U, Ericsson CG, Nelsson J, Svane B, Hamsten A, et al. Retardation of

coronary atherosclerosis: the Benzafibrate Coronary Atherosclerosis Intervention Trial (BECAIT) and other angiographic trials. Cardiovasc Drugs Ther 1997; 11:257-63.

69. Mishra SK, Rath PK, Mohanty NK, Mishra HN. Acute myocardial infarction in young patients. Indian Heart J 2003; 55(5): 359.

70. Puri A, Gilhotra HS, Singh S, Narain VS, et al. Smokers with premature coronary artery disease: Correlation with Novel Risk Factors. Indian Heart J 2003; 55(5): 414.

71. Patil CN, Christopher CP, Chakrapani M. A study of risk factors of acute myocardial infarction in young adults. KJMS 2005; 4(1): 44.

72. Ranjit N, Vehro NK, Vehro M et al. Acute MI in a young south Indian-based population; Curr Med Res Opin. 2002; 18(4); 242-8.

73. Kannel WB, D Agostino RB, Belarger AJ, Fibrinogen, Cigarettes, smoking and risk of cardiovascular disease: Insight from the framingham study, Am Heart J 1987; 133: 1006-10

74. Craveri A, Tornoyhi G, Paganardi L. et al., Hemorrheologic disordes in obese patients. Minerva med 1987; 78: 899-906.

75. Craro ML, Gloria LM, Slehub J et al. Hyperhomocystinemia in chronic

alcoholism : correlation with folate, vitamin B12 and vitamin B6 Am clin Nuir 63: 220-124.

76. Mennen LI, Baikav B, Vol S, Caces E, Eschwege E. Fibrinogen : a possible link between alcohol consumption and cardiovascular disease. DESIR study group. Arterioscles thromb vase Biol 1999; 19: 887-92.

PROFORMA

Name: I.P.No.: Age:

Sex: DOA: Occupation: DOD:

Address:

Diagnosis

Presenting Complaints Chest pain / Dyspnoea / Palpitation

History of presenting illness

Chest Pain

Site - Onset- Nature - Duration: Radiation - Continuous/intermittent

Severity - Aggravating/precipitating factors - Relieving factors

Dyspnoea

Duration /Onset/ Time of onset in relation to pain / NYHA Class / I/II/III/IV

PND / orthopnoea

Palpitations

Onset / nature/ duration/ Precipitating/Aggravating factors /Relieving factors

Past History

Diabetes Mellitus/ Hypertension / Dyslipidemia / Cerebrovascular accident

Thyroid disorder/ Rheumatic fever/ Liver disease /Renal disease.

PERSONAL HISTORY

Diet	-	vegetarian/non-vegetarian/mixed
Smoking	-	beedies/cigarettes
	-	duration
	-	number/day
Alcohol	-	duration
	-	quantity……../day
Tobacco chewing	-	Yes/No/ duration

Treatment History -

Family History

Coronary artery disease	-	Yes/No
Hypertension	-	Yes/No
Diabetes	-	Yes/No

Dyslipidemia - Yes/No

Sudden deaths - Yes/No

GENERAL PHYSICAL EXAMINATION

Condition of the patient - Wt (in Kg) - Ht (in length)

- BMI (kg/m2)

Icterus / Pallor/ Cyanosis/ Clubbing /Pedal edema /Lymphadenopathy

Vitals:

Pulse - / minute

BP - /mmHg in right upper limb

Respiratory rate - / minute

Pulse

Rate / Rhythm / Volume /Radio-radial/radio-femoral delay

Other peripheral pulses:

Blood pressure (R) UL (R) LL (L) UL (L) LL

Systemic examination:

1.Cardiovascular system

a. Inspection

Shape of the percordium -

Precordial pulsation/ Other pulsation -

Apical impulse -

b.. Palpation

Apical impulse-site -

Apical impulse-character / Parasternal heave / Thrill

c.Percussion

Cardiac borders

d.Auscultation

Mitral area /Tricuspid area / Aortic area / Pulmonary area

2.Respiratory system

Inspection /Palpation/Percussion/ Auscultation

3. Per abdomen

Inspection /Palpation/Percussion/ Auscultation

4. Nervous system

Hb, TC, DC, ESR, RBS , UREA,

S. CREATININE

Lipid profile- LDL/ HDL/ TGL

PLASMA FIBRINOGEN- mg/ dl

ECG:

Rate Rhythm P wave

QRS complex PR interval QRS complex ST segment

Echocardiography

LIST OF ABBREVIATIONS

ATP	Adult treatment panel
BMI	Body mass index
CAD	Coronary artery disease
DBP	Diastolic blood pressure
ECG	Electrocardiogram
HDL	High density lipoprotein
ICAM	Intracellular adhesion molecule-1
IHD	Ischemic heart disease
JNC	Joint National Committee
LDL	Low density lipoprotein
MI	Myocardial infarction
MTHFR	Methylene tetrahydrofolate reductase
NCEP	National Cholesterol Education Programme
NO	Nitric oxide
PAI	Plasminogen activator inhibitor
PVD	Peripheral vascular disease
SBP	Systolic blood pressure
t-PA	Tissue plasminogen activator
USA	United States of America
WHO	World Health Organisation

PATIENT CONSENT FORM

Study detail : "STUDY ON PLASMA FIBRINOGEN IN ACUTE MYOCARDIAL INFARCTION"

Study centre : THANJAVUR MEDICAL COLLEGE & HOSPITAL

Patients Name :

Patients Age :

Identification Number:

Patient may check ($\surd$) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ☐

I hereby consent to participate in this study. ☐

I hereby give permission to undergo complete clinical examination and diagnostic tests including haematological, biochemical, radiological tests. ☐

Signature/thumb impression:

Patients Name and Address: Place Date

Signature of investigator :

Study investigator's Name : Place Date

Sl.No.	Name	IP No.	Age yrs	Sex	Chest pain	Sweating	Vomiting	Breathlessness	Palpitation	Smoking	Diabetes mellitus	Hypertension	F - CAD	Alcohol	BMI (kg/m2)	RBS (mg%)	CK- MB (IU/L)	Lipid profile (mg%)				B.Urea (mg%)	S.creatinine (mg%)	P.fibrinogen (mg/dl)	ECG	ECHO	TREATMENT
																		TC	Trigl	LDL	HDL						
1	Murugaesan	1395932	33	M	Y	Y				y		Y		occ	25	144	38	220	170	130	56	34	1.1	440	IWMI	LV FN	thrombolysed
2	Pitchamuthu	1401941	25	M	Y									occ	23	102	42	133	86	72	44	30	0.9	420	ASMI	LVD EF50%	thrombolysed
3	Palanimanikam	1408493	36	M	Y	Y									21	170	60	170	140	92	50	24	0.9	480	EAWMI	LVD +MR	not thrombolysed
4	Ravichandran	1400506	41	M	Y					Y			Y	occ	22	129	145	240	295	131	50	28	1	294	ASMI	LV FN	thrombolysed
5	Suresh babu	1398653	30	M	Y										23	160	74	270	220	184	42	28	1.1	464	AWMI	LV FN	thrombolysed
6	Chellaiyan	1409078	40	M	Y					Y	y				22	168	42	148	88	86	44	32	0.9	448	ASMI	LVD EF50%	thrombolysed
7	Kaliyaperumal	1410197	42	M	Y	Y				Y		y			25	180	64	171	140	99	44	52	1.2	390	AWMI	LV FN	thrombolysed
8	Ravichandran	1415343	48	M	Y						ND			occ	23	320	64	160	85	90	53	40	1.1	334	IWMI	LVD EF60%	not thrombolysed
9	Selvam	1365388	36	M	Y					Y		ND			30	190	52	270	130	194	50	34	1	424	IWMI	LV FN	thrombolysed
10	Venkatesan	1378431	35	M	Y				Y	Y				cr	22	132	70	168	180	86	46	32	0.9	356	IWMI	LV FN	thrombolysed

11	Kajamaideen	1378804	38	M	Y	Y	Y			Y					24	156	38	175	126	97	53	35	0.9	416	IWMI	LV FN	thrombolysed
12	Sulaimaan	1378707	40	M	Y			Y		Y					29	146	183	220	200	133	47	24	1.2	487	EAWMI	LV FN	thrombolysed
13	Kumar	1379043	42	M	Y					Y	ND		Y	cr	21	258	95	260	216	179	38	49	1.2	484	IWMI	LVD EF60%	thrombolysed
14	Mohan	1382945	46	M	Y					y	y				25	158	70	148	110	80	46	40	1.3	394	AWMI	LVD EF55%	not thrombolysed
15	Lakshmanan	1377098	48	M	Y					Y	Y				27	250	90	154	140	77	49	36	0.8	440	AWMI	LV FN	thrombolysed
16	Kumaran	1365257	50	M	Y					y		y			26	150	70	152	100	96	36	30	1.1	280	ILMI	LVD EF50%	thrombolysed
17	Selvaraj	1365954	64	M	Y	Y				Y		ND		cr	27	178	76	240	200	135	65	25	1.1	455	AWMI	LV FN	not thrombolysed
18	Mohammed ismail	1366175	58	M	Y			Y		Y					24	107	60	148	88	86	44	20	1	442	AWMI	LV FN	thrombolysed
19	Tamil selvan	1366933	51	M	Y	Y				Y	y	Y			29	130	45	160	126	90	45	28	0.9	480	IWMI	LV FN	thrombolysed
20	Haseena begam	1369259	58	F	Y						y	y			31	126	146	180	86	113	50	22	1	488	AWMI	LVD EF48%	not thrombolysed
21	Puniyamoorthy	1370246	59	M	Y		Y			Y	y				27	182	66	171	80	110	45	26	1	476	ASMI	LV FN	thrombolysed
22	Thiyagarajan	1373215	58	M	Y							y		occ	23	170	80	154	120	88	42	25	1.2	398	IWMI	LVD EF45%	thrombolysed
23	Panjalai	1375473	42	F	Y						Y				28	152	42	196	82	124	46	42	1.1	532	IWMI	LV FN	thrombolysed
24	Bharkathnisha	1375375	45	F	Y						y				32	170	64	204	160	140	32	38	1.1	472	IWMI	LV FN	thrombolysed

25	Balakumar	1378253	53	M	Y			Y		Y			Y		21	104	34	169	110	102	45	24	1.3	338	EAWMI	LVD EF50%	thrombolysed
26	Pappathy	1379243	60	F	Y	Y						y			.24.6	130	115	142	224	57	40	69	1.2	372	ASMI	LV F N	thrombolysed
27	Jayakumar	1385235	45	M	Y					Y		ND		cr	24	80	64	236	200	143	53	28	1.2	486	AWMI	LV F N	thrombolysed
28	Andiyappasn	1387090	68	M	Y					Y	y				29	124	40	183	116	118	42	24	1.1	438	AWMI	LVD EF50%	not thrombolysed
29	Kuppusamy	1388141	57	M	Y					Y		y		cr	29	130	62	188	106	126	41	34	1	384	AWMI	LVD EF40%	thrombolysed
30	Arumugam	1389034	45	M	Y					Y				cr	26	156	195	215	170	125	56	30	1.1	397	IWMI	LV F N	thrombolysed
31	Manikkam	1390847	48	M	Y		Y		Y	Y	y			occ	30	136	130	250	200	170	40	38	0.9	290	ALMI	LV F N	thrombolysed
32	Dhanam	1391771	62	F	Y							y			29	156	60	154	126	87	42	40	1.2	310	IWMI	LVD EF55%	thrombolysed
33	Arumugam	1392229	60	M	Y							y		cr	28	186	70	181	110	117	42	26	0.8	390	ASMI	LV F N	thrombolysed
34	Muthusamy	1392375	76	M	Y					Y		y	Y	occ	28	137	140	190	165	114	43	22	1	442	IWMI	LVD EF50%	not thrombolysed
35	Mohandass	1394245	48	M	Y					Y					21	146	146	130	96	70	41	52	1.3	468	AWMI	LV F N	thrombolysed
36	Gandhi	1419752	62	M	Y			Y			y	y			30	180	58	173	206	92	40	36	0.9	510	ALMI	LV F N	thrombolysed
37	Vishwanathan	1418674	45	M	Y					Y		ND			25	215	265	180	116	106	50	23	1.2	426	ALMI	LVD EF45%	not thrombolysed
38	Kamaraj	1420513	56	M	Y				Y		y				28	105	160	166	140	96	42	38	1.5	370	AWMI	LV F N	thrombolysed

39	Iruthayamary	1419617	60	F	Y	Y									23	138	88	200	140	122	50	36	0.8	395	ASMI	LV FN	thrombolysed
40	Abdulkanni	1414855	68	M	Y					Y	y				31	230	56	188	88	132	38	28	1.1	446	AWMI	LVD EF45%	not thrombolysed
41	Balu	1395476	45	M	Y					Y	ND			cr	29	124	93	180	130	108	46	32	1.4	460	IWMI	LV FN	thrombolysed
42	Prabhakaran	1415127	59	M	Y										29	73	39	199	129	131	42	30	0.9	394	ILMI	LV FN	thrombolysed
43	Senthilnathan	1411150	49	M	Y						y			occ	28	185	153	184	210	83	59	22	0.8	448	AWMI	LV FN	thrombolysed
44	Rasu	1410483	49	M	Y					Y		ND			30	172	82	184	171	109	40	42	1.3	395	ASMI	LVD EF40%	thrombolysed
45	Rajakannu	1396826	70	M	Y						Y				29	210	76	169	138	100	41	34	1.1	482	IWMI	LVD EF40%	not thrombolysed
46	Dhanalakshmi	1397409	65	F	Y										29	95	68	138	110	74	42	22	0.8	280	AWMI	LV FN	thrombolysed
47	Habeeb rahaman	1400508	52	M	Y			Y						cr	29	112	74	158	110	98	37	20	0.9	484	IWMI	LVD EF50%	thrombolysed
48	Meenakshi	1400545	75	F	Y			Y							27	142	110	170	96	108	43	36	1.1	410	IWMI	LV FN	thrombolysed
49	Krishnamoorthy	1400525	52	M	Y					Y	y	y			30	138	50	208	158	138	39	23	1.2	398	IWMI	LV FN	thrombolysed
50	Sivabakiyam	1395178	61	F	Y							y			21	218	60	154	150	80	44	30	1	446	ALMI	LV FN	thrombolysed
51	Natarajan	1395486	74	M	Y	Y					y	y			26	130	115	241	224	157	40	69	1.2	465	ASMI	LVD EF45%	not thrombolysed
52	Suresh	1404683	31	M	Y										24	80	64	236	200	143	53	28	1.2	486	AWMI	LV FN	thrombolysed

53	Palaniammal	1396070	55	F	Y									21	124	40	153	116	88	42	24	1.1	390	AWMI	LV FN	thrombolysed
54	Akbar hussain	1395811	54	M	Y					Y		y		cr	30	130	62	188	106	126	41	34	1	448	AWMI	LVD EF40%	thrombolysed
55	Paneerselvam	1396649	45	M	Y					Y				cr	27	156	195	215	170	125	56	30	1.1	450	IWMI	LV FN	not thrombolysed
56	Selvaraj	1396797	55	M	Y		Y		Y	Y				occ	31	136	130	256	200	176	40	38	0.9	462	ALMI	LV FN	thrombolysed
57	Ganesan	1396701	65	M	Y					y	y				31	156	60	184	126	117	42	40	1.2	460	IWMI	LV FN	thrombolysed
58	Natarajan	1398275	57	M	Y							y		cr	23	186	70	171	110	107	42	26	0.8	382	ASMI	LV FN	thrombolysed
59	Muthayan	1398705	65	M	Y					Y			Y	occ	27	137	140	170	165	124	43	22	1	420	IWMI	LVD EF45%	thrombolysed
60	Pounammal	1398413	50	F	Y										24	146	146	136	96	76	41	52	1.3	376	AWMI	LV FN	thrombolysed
61	Kunjammal	1398491	65	F	Y			Y							21	180	58	179	206	98	40	36	0.9	506	ALMI	LVD EF40%	not thrombolysed
62	Ulaganathan	1398574	52	M	Y					Y	y				28	215	265	181	116	108	50	23	1.2	344	ALMI	LVD EF45%	not thrombolysed
63	Sivamani	1398910	54	M	Y				Y			y			24	105	160	174	140	104	42	38	1.5	382	AWMI	LV FN	thrombolysed
64	Saroja	1406988	51	F	Y	Y									30	138	88	190	140	112	50	36	0.8	332	ASMI	LV FN	thrombolysed
65	Abdulsamath	1406860	50	M	Y					Y					28	230	56	137	88	82	38	28	1.1	462	AWMI	LV FN	thrombolysed
66	Swaminathan	1405987	50	M	Y					Y				cr	28	124	93	174	130	102	46	32	1.4	446	IWMI	LV FN	thrombolysed

67	Indirani	1408306	60	F	Y						y	y			26	73	39	193	129	126	42	30	0.9	438	IL MI	LV FN	thrombolysed
68	Ganapathy	1409480	47	M	Y					Y				occ	23	185	153	199	210	98	59	22	0.8	304	AW MI	LVD EF45 %	not thrombolysed
69	Pethuraj	1404684	53	M	Y		Y			Y		y			21	172	82	180	171	106	40	42	1.3	462	AS MI	LVD EF40 %	thrombolysed
70	Ponraman	1408570	65	M	Y						Y	y			23	210	76	176	138	108	41	34	1.1	398	IW MI	LV FN	thrombolysed